Irritable bowel syndrome.
Assessment of psychopathology
and its impact on the symptom complex.

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ABSTRACT

This thesis describes the assessment of depression and anxiety by questionnaire and visual analogue scale in patients with irritable bowel syndrome (IBS). It examines the relationship between such assessments and self-reported symptoms before and after a placebo controlled, double-blind trial of fibre supplementation in 49 IBS patients, and finds that a high depression score at outset may be a predictor of continuing symptoms regardless of treatment. The treatment itself was no better than placebo, though there was a substantial 'placebo' effect.

I consider the use of putative biochemical markers of 'stress' in such patients, but find that neither salivary IgA nor urinary metanephrine correlate well with symptoms, symptom response, or psychometric assessment scores. Platelet serotonin levels did not distinguish IBS subjects from those with other chronic gastrointestinal complaints. It seems unlikely that any of these parameters will be helpful in routine diagnosis or management of IBS.

A second cohort of IBS subjects was studied five years after initial diagnosis, using similar psychometric assessments. The chronic nature of the disorder was confirmed. The results suggest that anxiety levels might be an important influence on the longer-term maintenance of the symptom complex.

Finally the thesis examines aspects of the general practitioner consulting behaviour of a group of IBS patients. Such behaviour seems relatively stable over the longer term although there was a very high prevalence of diagnoses of depression or anxiety, both before the IBS diagnosis and during the five years to review.

The studies are considered to support a holistic approach to IBS; its pathogenesis, management, and natural history. The symptom complex is forged by the action of several factors, notably psychological, physical and circumstantial (life events). The behavioural and emotional elements of the symptom complex are best considered as one product, and the doctor-patient relationship plays an important modulating role. There is some evidence that depressed mood may be more important in determining short term responses, such as consulting behaviour, and anxiety in maintaining the perception of 'symptoms' in the longer term. Simple assessment of depression and anxiety, perhaps by 'user friendly' visual analogue scales, might usefully be incorporated in the routine assessment of IBS patients.

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Dedication

The thesis would not have been completed but for the forebearance of my family, Jane, Peter and Andrew, to whom it is dedicated.

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INTRODUCTION

CONCLUDING DISCUSSION

INTRODUCTION

The symptom complex now termed irritable bowel syndrome (IBS) has been recognised for many years. Powell (1820) provided the first written description of the syndrome ; '*occasional pain in the intestines and derangement of their powers of digestion with flatulence and a sense of suffocation*'. Around the turn of the century studies of '*membranous enteritis*' and '*membranous colitis*' were reported by Da Costa (1871) and White (1905) respectively. Allbutt (1884) described 139 cases of '*neurosis of the viscera*'. Hawkins (1906) noted that such conditions had no organic cause and were not helped by surgery. Bockus et al (1928) considered that many patients with '*neurogenic mucous colitis*' displayed evidence of psychoneurosis.

Peters and Bargen (1944) coined the name irritable bowel syndrome and commented that the increased incidence of IBS in the war years might be evidence of an association with stress. In subsequent years Almy (1951) again noted the frequency of neurotic traits, and developed experimental models aimed at testing the hypothesis of a link between stress and altered motility of the GI tract. Chaudhary and Truelove (1962) further described the syndrome emphasising the importance of psychological factors and the chronic nature of the condition.

IBS is a common diagnosis in gastrointestinal practice. Ferguson et al (1977) reported that in almost fifty per cent of patients referred to a gastrointestinal outpatient clinic the diagnosis was of IBS. In 888 of 2000 consecutive referrals to a gastrointestinal clinic the diagnosis was of functional disorder, of which IBS accounted for half (Harvey et al 1983). Switz (1976) confirmed that functional disorder was the most frequent diagnosis in patients referred to gastroenterologists in the developed world. Despite the frequency with which it is encountered, IBS remains an enigma, its aetiology unestablished, its treatment often difficult and contentious.

Insight into IBS has been greatly disadvantaged by poor definition of the syndrome and by a dualistic conflict over its likely aetiology. The symptom complex is considered by some to be the result of gastrointestinal dysfunction, perhaps dysmotility, though the precise nature of the organic disorder is not yet established (Grant Thompson 1984a, Kumar and Wingate 1985). To others IBS is a manifestation of psychiatric disturbance (Hislop 1971). The medical model of illness, to which most physicians owe historical (if not intellectual) allegiance, does not easily accomodate both these positions. Yet it has long been recognised that complaints and symptoms do not always have an explanation in physical disorder (Cabot 1907). Such symptoms are said to arise from 'functional disorder' and are frequently encountered in medical practice.

The concept of 'functional disorder' is itself poorly defined and it can be argued that the availability of this diagnostic label has further hindered understanding of IBS. The absence of organic disease does not imply that the symptoms have their origin in psychiatric illness (Bridges and Goldberg 1984); but neither does the absence of psychiatric illness or 'symptoms' imply psychological normality.

The 'symptom complex' and its assessment are the starting points common to the patient and to the consulted physician. For the patient the assessment fires the process by which the experience may give rise to symptoms, and to seeking medical attention. For the physician the assessment of gastrointestinal tract function is central to the diagnostic process instigated by the patients attendance. For both participants the eventual formulation will carry significant implications for future behaviour.

The relationship between reported symptoms and objective measures of gastrointestinal function is not well established. Eastwood et al (1984) confirmed a relationship between constipation and increased enteric transit time, a finding demonstrated by Cann et al (1983), who also described a reduction in whole gut transit time associated with diarrhoea. An altered small bowel motility pattern was said to coincide with symptoms (Kellow and Phillips 1987). However Oettle and Heaton (1987) found poor correlations between colonic symptoms, intestinal transit time, and stool weight over a 28 day period. Hillman et al (1982) found no relation between reported symptoms and objective measures of diarrhoea and constipation. Whitehead et al (1980) found no correlation between changes in myoelectric activity induced by rectosigmoid distension and the severity of symptoms. Despite this variable correlation between symptoms and enteric events, in the absence of any

distinctive biochemical or physiological characteristic, the definition and diagnosis of IBS must be based on reported symptoms.

The symptom complex is dominated by abdominal pain and a change in bowel habit. Clinical studies have focussed on differentiating IBS from organic disease and on classifications of the syndrome according to symptom patterns. IBS is frequently subdivided into constipated, diarrhoeic, or alternating types. Such a classification is greatly limited by the wide variation in interpretation of bowel habit and its description, and by the variability of bowel habit disturbance in individual patients across time. Some still regard the diagnosis as one of exclusion (Sammons and Karoly 1987) but there is now general agreement that the diagnostic process can be a positive one.

This positive diagnostic process has been advanced by Manning et al (1978) who define the gastrointestinal symptomatology in IBS. In discriminating IBS from organic disease the symptoms with greatest power are :

1. abdominal distension (as evidenced by tight clothing or visible appearance).
2. pain relief with bowel action.
3. more frequent stools with onset of pain.
4. looser stools with the onset of pain.

At least two of these symptoms are present in 91 per cent of patients with IBS but in 30 per cent of those with organic disease. In only seven per cent of IBS patients were none of these symptoms reported : 52 per cent of those with organic disease denied all of these symptoms.

Kruis et al (1984) proposed a diagnostic score based on an analysis of 479 patients. Using the weighted score at a sensitivity of 83 per cent, the specificity was 97 per cent. Unlike Mannings' system, the Kruis scoring system incorporates laboratory results as well as reported symptoms.

While such systems may distinguish IBS from organic gastrointestinal disease in clinic patients, the experience of a unique constellation of gastrointestinal events does not distinguish patients with IBS from 'normal' subjects in community surveys of bowel function. Up to 35 per cent of 'normal' people report gastrointestinal experiences indistinguishable from those of IBS sufferers in surveys of the general population (Thompson and Heaton 1980, Drossman et al 1982). Almost half the 'normal' population reported a significant 'bowel' dysfunction, defined as :

1. alternating bowel habit more than 25 per cent of time.
2. at least six episodes of abdominal pain in the preceding year with three or more of the following characteristics ; relief by defaecation, loose stools with the pain, more frequent stools with the pain, abdominal

distension, mucus in the stool, or incomplete evacuation.

3. constipation ; straining at stool, or less than two stools per week.
4. diarrhoea ; loose or watery stools for more than 25 per cent of the time, or more than 21 stools per week.

These are precisely the components of the IBS symptom complex ; but a minority of people with this gastrointestinal experience profile become IBS patients (Thompson and Heaton 1980, Whitehead et al 1982). It is recognised that increased symptom severity increases the likelihood of seeking medical attention in some circumstances, notably where anxiety or depression is the dominant complaint (Ingham and Miller 1983). However there is little to support the proposition that symptom severity is the factor which distinguishes IBS symptom reporters (patients) from IBS suffering non-reporters.

Coincident symptoms might be a factor in determining that the experience of the IBS gastrointestinal symptom complex precipitates seeking medical attention. Non-gastrointestinal symptoms are common in IBS (Whorwell et al 1987). Maxton et al (1989) confirmed a high prevalence of non-colonic symptoms in 100 IBS patients. Almost half the patients rated such a non-colonic symptom as the most troublesome for them. It is not clear whether IBS 'non-patients' share this additional, non-gastrointestinal symptom profile. It is characterised by complaints such as tiredness, lethargy, and headache,

as well as genitourinary symptoms such as urinary frequency and dyspareunia.

IBS therefore seems to be a dimensional disorder, there being a continuum of experience with no clear line of delineation between patient and non-patient. Although the dominant complaints are most frequently gastrointestinal, patients often acknowledge troublesome non-gastrointestinal symptoms. It seems possible to reach a diagnosis positively by analysis of the symptom complex and simple clinical examination.

The transition from experience to symptom, and the reasons for seeking medical attention, are central themes of illness behaviour theory. This shifts the emphasis from the standpoint of the traditional medical model - *what is wrong ?* (a structural approach), to an approach which rather asks - *why is this individual behaving in this way at this time ?* (a functional approach).

It has been argued that those who seek medical advice are distinguished from non-seekers with similar experiences by a disturbed sense of well-being. Where an individual considers that a threat to well-being exists, the response is generally to bring into play strategies which serve to minimise the disruption and distress. Such strategies may be behavioural and/or emotional. Consulting the doctor can be seen as one such response or 'coping strategy'.

A vast literature attests that cultural and psychosocial factors influence help-seeking (or consulting) behaviour. Behavioural studies have shown ethnicity, family structure, personal attitudes and values, informal social influences, and access to care, to be among the most powerful of such influences. However field studies often find much less vigorous associations between such factors and consultations. Mechanic (1979) considers why this apparent conflict might arise in methodological and conceptual differences, but these limitations must

be considered when interpreting such studies.

Andersen and coworkers (Andersen and Newman 1973) have described a model which seeks to explain the great variability in consulting behaviour. They propose that the factors which modulate consulting can be divided into three sets.

Predisposing factors are those which exist before the onset of the 'illness'. Those most often cited are demographic (age, sex, and marital state), social (class, educational attainment, occupation), and attitudes and beliefs. The contradictory literature is well exemplified here - social class and educational level have been found to be associated (Ingham and Miller 1983) and not associated (Wolinsky 1978) with the likelihood of consulting. However there is a concensus that women consult more frequently than men but that this reflects need factors as well as an increased disposition to seek reassurance from doctors (Briscoe 1987). Consultation rates increase with age from the late teens but this may reflect the increased likelihood of disease states (circumstances which provoke the response) rather than changes in predisposition. This distinction may be equally important for other factors.

Enabling factors are those concerned with the availablity of services. This set includes cost (and its relation to income) and geographical distance. Clearly many of the social *predisposing factors* will impinge here.

Need or *illness factors* are those which concern the immediate cause of the putative consultation. Symptom severity is an important determinant of consulting behaviour (Ingham and Miller 1983), as is symptom chronicity. But symptom severity does not necessarily correlate with the degree of distress engendered, and perceived seriousness is a further influence on help-seeking behaviour (Hulka 1972).

Perception and evaluation are clearly delineated in Andersons' conceptual framework. In other work evaluation is subdivided into interpretation and attribution and still others use 'evaluated illness' synonomously with 'diagnosed illness' (Banks et al 1975).
Psychiatric morbidity is well established as an important determinant of consultation (Barsky et al 1986, Williams et al 1986, Vasquez-Barquero et al 1990).

In the context of irritable bowel syndrome the factors which are preeminent influences on the perception, interpretation and attribution of the symptoms, and on the development of the consulting response, can usefully be considered in 4 domains which overlie the predisposing, enabling, and need sets:

1. The nature of the potentially destabilising event.
2. The psychological profile of the individual.
3. Previous experience of this and other events.
4. The circumstances in which this interaction is occurring.

Each of these domains is now discussed in relation to the aetiology and natural history of IBS.

The nature of the potentially destabilising event

Intestinal dysmotility

Gut spasm is an attractively simple explanation for the symptoms in IBS, particularly abdominal pain. It has long been recognised that in IBS patients symptoms can be provoked by changes in intraluminal pressures in the small intestine or colon produced by inflation of balloons (Holdstock et al 1969). Ritchie (1973) demonstrated that rectosigmoid distension to 60ml at 35cm from the anal margin caused pain in 55 per cent of IBS patients but in only six per cent of controls. Distension in the colon had a similar profile of response (Ritchie 1973, Whitehead et al 1980). Swarbrick et al (1980) and Moriaty and Dawson (1982) showed that distension of other sites, including the oesophagus and the small intestine, caused pain.

Abdominal pain is such a dominant symptom in IBS that it has been the subject of much study. The site of the pain is extremely variable, occurring in many positions in the abdomen (Chaudhary and Truelove 1962), and at extra-abdominal sites. Pain has been reported in the chest, lumbar spine, sacroiliac joints, and thighs (Holdstock et al 1969). Frequently many sites are involved. Pain may be continuous or colicky, or both (Chaudhary and Truelove 1962). With enteric distension the pain tends to be felt in the midline in normal controls, but in IBS patients it can be located anywhere in the abdomen

(Swarbrick et al 1980, Moriaty and Dawson 1982). The site of the distension does not predict the site of the pain. The distension-provoked pain is similar in character and position to their usual pain in 50 per cent of IBS patients (Swarbrick et al 1980).

In one study distension pain threshholds were lower in IBS patients than controls (Ritchie 1973). Colonic hyperalgesia, in which there is greater perception of noxious colonic stimuli, was a suggested explanation. Latimer et al (1979) could not reproduce the findings of reduced pain threshhold to colonic distension in IBS patients, reporting a linear correlation between pain and distension in IBS subjects, in normal controls, and in psychologically disturbed patients in whom gastrointestinal symptoms were not a feature. Latimer et al criticised the controls used by Ritchie, many of whom were constipated. Cook et al (1987b) reported that IBS patients had greater pain tolerance to electrocutaneous stimulation than normal subjects. Interestingly a group of Crohns disease patients also had higher pain tolerance than the controls. This argues against the suggestion that IBS patients might overperceive abdominal experience or magnify the pain ; 'somatic amplification' (Barsky 1979).

Nor is there evidence to suggest that IBS patients are habitually subject to unusually great distension as a consequence of increased enteric gas production. Lasser et al (1975) found similar rates of production and

composition in 18 IBS and 10 control subjects. This is not to exclude a possible role for enteric gas - clearly its' production and composition, to a large extent dependent on diet, may have profound influences on enteric motility patterns.

Colonic motility.

Colonic motility studies are beset with difficulties of methodology and terminology. There are three main types of mechanical activity (contractions):

1. segmental contractions
2. propulsive contractions
3. mass movements

Colonic contractions are brought about by electrical activity within the smooth muscle of the bowel wall. There are two electrical wave rhythms in the colon:

i. 3 cycle / minute slow wave activity, intrinsic and intermittent.

ii. 6-12 cycle / minute activity.

Contractions occur only if the action potential discharge coincides with slow wave activity. Although no single characteristic pattern of myoelectric activity unique to IBS has been identified, several abnormalities occur with greater frequency or to a greater degree in IBS subjects than in controls :

(1) Alterations in slow wave 3 cycle / min activity.

Chaudhary and Truelove (1961) reported that colonic motility was increased in IBS patients with constipation though other studies failed to confirm this (Snape et al 1977). Trotman and Misiewicz (1988) found sigmoid hypomotility. Whitehead et al (1980) described gastrointestinal tract motility in 28 IBS patients. The colon and small intestine seemed hyperactive in IBS, but not under resting conditions. In the colon slow contractions of at least 15s duration occurring irregularly were more frequent in IBS (both diarrhoeic and costive types). Fast contractions were more common in diarrhoeic type only.

Sarna et al (1982) referred to electrical control activity (ECA), which is equivalent to slow wave activity, as the basic myogenic phenomenon. ECA modulates electrical response activity (DERA) which are spike bursts responsible for rhythmic contractions. In the colon ECA is irregular. They failed to confirm increased ECA (3 cycle / min activity) in IBS patients. Welgan et al (1985) likewise found no difference in 2-4 cycle / min slow wave activity. Frexinos et al (1987) found reduced or absent short spike bursts (SSB) (equivalent to the DERA of Sarna). He also reported an increase in the total number of migrating long spike bursts (MLSB) after eating in painless IBS of diarrhoeic type. Bueno et al (1980) described three groups of colonic motor disturbance including SSB of high amplitude which were said to occur with bouts of pain.

(2) Increased contractions at 3 cycle / min (Sullivan et al 1978).

The abnormally high incidence of slow waves (3 cycle / min), possibly related to pressure waves, was confirmed by Taylor et al (1978). Segmental and nonpropulsive, such waves were also found in non-IBS subjects. The abnormality persisted for upto 18 months even with symptomatic improvement, which occurred in 12 of 20 patients who were free of symptoms after one to three months treatment with bran or antispasmodic.

(3) Increased activity in response to various stimulants (Whitehead et al 1980).

Snape et al (1978) showed increased slow wave activity in IBS patients only when stimulated by pentagastrin or cholecystokinin. There was no increase in basal contractions of the same frequency.

(4) Delayed postprandial colonic motor response.

The post prandial colonic spike and motor activity is delayed in IBS (Sullivan et al 1978). The effect is diminished by an anticholinergic agent (clidinium). Misiewicz et al (1966a) previously showed decreased postprandial activity upto 30 minutes after a meal.

Small bowel motility.

Small bowel transit time was variably reported as reduced or normal in IBS (Corbett et al 1981). Cann et al (1983) reported that small bowel transit time

was reduced in diarrhoeic-IBS, but increased in constipated-IBS. There was no significant difference in gastric emptying. Of 34 patients who complained of pain during the meal transit, the pain was associated with arrival of the meal in the caecum in 74 per cent. Other symptoms often occurred simultaneously : nausea, abdominal distension, and urgency to defaecation.

Early studies suggested reduced small bowel motor activity in IBS during pain, though there was no change when asleep or during normal activity (Horowitz and Farrar 1962). In the small bowel, during fasting, intermittent contractions interupt a relatively quiescent background with occasional migrating motor complexes (MMC). MMC travel distally from the proximal jejunum for a variable distance. Postprandially, irregular random contractions are the rule. There is great variation in the periodicity and duration of MMC in health (Kerlin and Phillips 1982) and in IBS (Kingham et al 1984). Kellow et al (1988) demonstrated changes in motor activity in the small bowel in continuous recordings of upto 29 hours duration. There was no difference between the IBS and control subjects in MMC speed or in distance propagated distally in the small bowel. In diarrhoeic-IBS subjects the MMC reached the ileum more often, and the interval between MMCs was shorter, than in constipated-IBS subjects. Prolonged propagated contractions were associated with pain in all 12 of the IBS subjects in whom they were recorded, and in three of six controls in whom it occurred. The pain was described as similar to their usual pain in the IBS sufferers. Non-propagating

contractions occupied more of the quiescent phase in IBS subjects, in whom maximum pressures were higher. These last two observations were not associated with the occurrence of pain.

Kellow et al (1988) further suggest that stimuli may unmask dysmotility in IBS subjects. There was an increased small intestine motility response to several stimuli in IBS patients compared to controls. The changes precipitated by a fatty meal, infusion of cholecystokinin octapeptide, or ileal distension, were more notable in subjects with diarrhoeic IBS.

Oesophageal motility.

Smart and Atkinson (1987) showed abnormalities in oesophageal motility in IBS patients who did not have particularly prominent oesophageal symptoms. Lower oesophageal sphincter pressure was significantly reduced as in a previous study (Whorwell et al 1981) but there was no abnormality of oesophageal motility. Surprisingly 80 per cent of their 25 patients had evidence of inflammatory oesophageal disease but there was no correlation between severity of these changes, symptoms, and the degree of pH monitored gastrooesophageal reflux. In view of this suggestion of abnormal vagal function in IBS and the high prevalence of other putative autonomic dysfunctional conditions in the families of IBS patients (notably migraine), some authors have postulated an underlying generalised disturbance of autonomic function (Esler and Goultson 1973).

The nature of the potentially destabilising event.

Changes in intestinal motility with stress.

Stressful conditions, emotional and physical, seem to increase colonic pressure activity in IBS patients (Narducci et al 1985) and in healthy normal individuals (Almy et al 1949). Stress increased the proportion of 2-4 cycle / min slow waves in IBS, while in normals the proportion was decreased despite the similarity in the resting state (Welgan et al 1985). Physical stress seemed to increase the gastrocolic response to a meal, though here emotional stress seemed to decrease the sigmoid colon pressure response. Narducci et al (1985) noted adaption to the stress, a repeated exposure evoking little increase in colonic motility in normal subjects. Surprisingly this adaptability was not examined in IBS subjects. Oral benzodiazepine seemed to ameliorate the effect of stress in IBS patients, although the potential influence of the adaptive response renders interpretation difficult.

Acute emotional stress increases upper oesophageal tone. This manifests as globus hystericus - a well recognised phenomenon, though the mechanism is unestablished (Cook et al 1987a). Patients with nutcracker oesophagus or noncardiac chest pain have distal oesophageal contractions of greater amplitude than controls when exposed to psychological stress, though not under resting conditions (Richter et al 1986). Pain induced by cold immersion

of the hand slows liquid gastric emptying (Thompson et al 1986), while dichotamous listening stress appeared to have little effect (Cann et al 1983a). Roth et al (1953) could find no characteristic change in small intestinal motility during emotional stress within the context of a psychiatric interview. Nor were symptoms correlated with motility changes. Emotional stress (dichotamous listening) has been reported to reduce fasting MMCs (McRae et al 1982), and to reduce small bowel transit time. In IBS patients MMCs were reduced by stress, as they were in normal and in disease controls (Kumar and Wingate 1985). Abnormal irregular contractions during stress seemed to coincide with symptoms in IBS patients.

Involvement of non-gastrointestinal systems in functional disorders is well documented. Symptoms such as headache, insomnia, dyspareunia, and palpitations are frequently reported in IBS (Kirsner and Palmer 1958, Fielding 1977, Whorwell et al 1986a). There is evidence to suggest that symptoms may result from disorders of smooth muscle in non-enteric structures (Whorwell et al 1986b). There is a much increased incidence of bladder dysfunction (in urodynamic studies) in IBS patients compared to controls. Detrusor instability is the most common disorder. It is not clear whether this has clinical significance, but the same group reported an increased incidence of urinary symptoms, notably frequency, urgency and nocturia in IBS subjects. (Whorwell 1986a).

The concept of the 'brain-gut' link has been suggested as a model for the disturbances which might provoke the IBS symptom complex :

Disorder of smooth muscle or enteric nervous system is suggested by the evidence of altered myoelectric response to various stimuli, and altered smooth muscle function elsewhere. In this regard it is notable that although myoelectric response to cholecystokinin is exaggerated in IBS, no clear differences (qualitative or quantitative) in regulatory gut peptides have been demonstrated when comparing IBS subjects with normal controls (Besterman et al 1981).

A central dysfunction is supported by the effects of psychological stress in IBS and by the importance of arousal in the abnormal motility and symptom profiles (Kellow and Phillips 1987).

Overall no motility pattern specific to IBS sufferers has been established, either at rest or when patients are subject to various experimental stresses. There is no convincing evidence that a unique disturbance of gastrointestinal motility underlies the symptom complex in IBS. Such changes that are found do not readily explain nonenteric symptoms (Snape et al 1977, Taylor et al 1978, Latimer et al 1981).

The nature of the potentially destabilising event.

The influence of diet : fibre content.

Although an increased incidence of IBS during wartime was reported in the English literature, Boas (1926), writing in the German literature, described how mucous colitis had become less common during the war. He suggested that this might be attributable to dietary changes, the wartime diet containing more residue and less meat. Dietary fibre is often recommended as treatment for IBS (Manning et al 1977) and is thought by some to be protective against development of the symptom complex (Mendeloff et al 1979). But the evidence in favour of this approach is not overwhelming.

Fibre is a generic term describing several substances which have in common a propensity to increase stool weight and reduce gastrointestinal transit time (Kay 1982). This effect is achieved in one of two ways :

(1) an increase in faecal water content. Cereal fibre is thought to act in this way, a property it owes to its structure rather than to its chemical composition (Robertson and Eastwood 1981).

(2) an increase in the bacterial content of the stool, by which vegetable fibre increases stool bulk (Stephen and Cummings 1980).

Were lack of dietary fibre, absolute or relative, a major factor in the maintenance of the IBS symptom complex, one would expect IBS patients to eat less dietary fibre than otherwise matched controls. This has not proven to be the case. Dietary histories suggest no consistent shortfall in dietary fibre intake in IBS patients compared to healthy controls (Hillman et al 1982, Fielding 1979). Likewise there is no difference in transit time or stool weight between IBS and controls (Goy et al 1976, Eastwood et al 1984, Hillman et al 1982).

Such studies are confounded by the extreme variability of colonic function within the normal, healthy population (Wyman et al 1978, Drossman et al 1982). Factors such as transit time, wet and dry faecal weight, faecal volume, and frequency of defaecation show enormous inter-individual variability and great intra-individual, day-to-day variability (Wyman et al 1978). This may reflect true variation in experience but might be a consequence of poor reproducibility of the method(s) of assessment (Eastwood and Kay 1979). A further confounding factor is the influence of psychological factors on stool characteristics ; personality profiles may predispose to low stool volume (Hillman et al 1982, Tucker et al 1981).

The nature of the potentially destabilising event.

The influence of diet : food intolerance

Dietary constituents have been implicated in the IBS symptom complex throughout the literature. In Chaudhary and Trueloves' (1962) seminal paper 44 per cent of patients reported a connection between symptoms and some foodstuffs. In uncontrolled studies a gluten free diet improved symptoms (Pock-Steen 1973) though there is no evidence of coeliac disease in IBS patients. Nor is there evidence that lactase deficiency can account for symptoms in more than a very small minority of cases. Lactose intolerance is characterised by symptoms similar to those which occur in IBS. Intolerance does not effect all those who have lactase deficiency ; in part this is related to the dose dependant nature of the symptomatology. Lactase deficiency is relatively common and most studies suggest that it is not found more frequently in IBS patients than in the general population (Ferguson et al 1984, Pena and Truelove 1972).

Alun Jones et al (1982) described how 14 of 21 patients with abdominal pain and diarrhoea felt that their symptoms improved with avoidance of certain specific foodstuffs. Six patients were subsequently challenged double-blind with their offending foodstuff and were able to identify 10 of the 12 challenge and control periods correctly. Rectal PGE2 was increased on the challenge

days and for upto 48 hours thereafter. The paper does not include details of the response in other than general terms, nor any indication of symptom duration. All patients certainly had diarrhoea. There was no psychological assessment. In another study, 36 of 49 patients with suspected food intolerance did not respond to a 'nonallergenic' diet. In eight patients a specific foodstuff was identified but in only two patients was the diagnosis sustained after blind challenge (Farah et al 1985).

McKee et al (1987) studied a more diverse group of IBS patients. 40 patients showed little change in symptoms during an exlusion diet. 15 per cent responded symptomatically, though a further 12 per cent reported general improvement. The response rate was certainly best in those with predominantly diarrhoea. Exclusion diets are perhaps applicable in a minority of IBS patients in whom diarrhoea is the main complaint. Two hundred patients in whom other treatments had failed were treated with an exclusion diet (Nanda et al 1989). 48 per cent of the 189 who completed the three week period reported symptomatic improvement. 80 per cent of these responders were able to identify specific symptom-precipitating foodstuffs in a subsequent nonblind challenge. The absence of a placebo group, the short initial treatment period, and the non-blind nature of the rechallenge make firm conclusions difficult. No details are given of psychopathology, which one would expect in a proportion of such a large group said to have failed to respond to conventional therapy.

Bentley et al (1983) studied 27 patients with 'food allergy' and a mean symptom duration of five years. Seven patients reported no change in symptoms on an exclusion diet, or on subsequent food reintroduction ; four no consistent change ; and ten a consistent exacerbation by certain foodstuffs. In eight double-blind investigations, three diagnoses of food intolerance were substantiated. However in two cases there was already established milk intolerance, and all three cases were atopic by conventional criteria. 14 randomly selected patients were assessed by an independent psychiatrist using a standardised interview schedule. 12 had scores on the interview schedule indicative of psychiatric disorder ; in nine the diagnosis was neurotic depression.

Pearson et al (1983) examined 23 patients who were attending an allergy clinic and who attributed symptoms to food allergy. The diagnosis was confirmed in four who each had typical atopic symptoms. In the remainder there was a high incidence of psychological disturbance, assessed by interview schedule. The most common diagnosis (10 patients) was of depression. Rix et al (1984) describe the psychiatric symptomatology in this group of patients and comment that prognosis seemed to be related to the strength of belief that food allergy was responsible, and that this might be critically influenced by the investigative process.

Fructose and sorbitol are natural constituents of many foods which seem to be malabsorbed in many normal subjects. The malabsorption can cause symptoms, particularly if the sugars are given together, which resemble the IBS symptom complex. In IBS patients the symptoms so produced seem more severe than in normal controls, though the prevalence of fructose malabsorption seems no greater in IBS patients (Rumessen and Gudmand-Hoyer 1988).

Although alcohol has a laxative effect and is associated with dyspepsia (Langman et al 1982), there is little to suggest that alcohol abuse accounts for many cases diagnosed as IBS. However few studies have specifically assessed the possible contribution of alcohol to the IBS symptom complex.

Prolonged, probably post-infective, diarrhoea precedes the diagnosis of IBS in perhaps one quarter of sufferers (Chaudhary and Truelove 1962). It is not clear whether the diarrhoeic episode is simply the precipitant of medical attention seeking in previous non-reporters.

It has recently been suggested on the basis of a preliminary study of four patients that a gonadotrophin-releasing hormone (GnRH) agonist might prove a useful treatment for IBS and provide insight into a possible neuroendocrine pathophysiology (Mathias et al 1989).

The psychological profile of the individual.

Several of the earliest papers describing IBS refer to emotional factors such as anxiety, nervous tension, neuroses, and guilt (Bockus et al 1928, White 1905, Allbutt 1884, Powell 1820). In their landmark paper Chaudhary and Truelove (1962) remarked that among the factors which appeared important in the genesis of IBS, psychological factors stood preeminent ; at least one such factor was present in 103 of the 130 patients. They also observed that almost all patients showed at least some measure of improvement, and that those patients in whom psychological factors were present fared worse, except where there was a major change for the better in their life situation, when the prognosis was much improved.

Psychiatric illness.

On the basis of a study of 14 patients Bouchier and Mason (1979) proposed a classification of IBS patients based on two distinct psychological profiles. In one class the gastrointestinal symptoms seemed a response to life changes or stress. In the other the symptoms were one manifestation of chronic psychological illness, predominantly depression. Hislop (1971) took this further, arguing that IBS is an affective disorder. He compared 67 patients with 67 controls from a casualty department. 65 patients in the IBS group had evidence of depression or anxiety neurosis.

Gomez and Dally (1977) examined all patients presenting to a gastrointestinal clinic who were not accorded an organic diagnosis. On the basis of clinical judgement they suggested that all 96 such patients with 'functional disorder' were psychologically disturbed, though the nature of the disturbance was not always well defined. 32 per cent were depressed, 'chronic tension' was the diagnosis in 32 per cent, and hysterical states accounted for 18 per cent of the diagnoses. There was no control group. Yet most authors do not find evidence of psychiatric illness in all IBS sufferers.

The use of more structured tools for psychiatric diagnosis and of a control group is no guarantee of greater validity of the conclusion. Liss et al (1973) and Young et al (1976) describe studies using a structured psychiatric interview from which diagnoses are derived using Feighners criteria (Feighner et al 1972). 72 per cent of 29 IBS patients (average age 44) had psychiatric illness, most frequently depression or hysteria, compared with 18 per cent of controls drawn from a medical clinic. However Feighners criteria give great diagnostic weight to physical symptoms, having been designed for use in the diagnosis of hysteria in young patients. The significance of such physical symptoms for psychiatric diagnosis may be much less in IBS patients. This difficulty is often encountered when using structured questionnaires for the diagnosis of depression, such is the weight given to physical symptoms in most such scales.

The Hospital Anxiety and Depression Scale attempts to address this difficulty, by diminishing the impact of somatic symptoms on the assessed probability of depression or anxiety state (Zigmond and Snaith 1983). However this may be to miss some of the point where the contention is that the the somatic manifestations are the only or predominant manifestations of psychological disturbance.

Rose et al (1986) used the Depression Inventory (Beck et al 1961) to estimate the prevalence of depression in outpatients with functional abdominal pain. He reported that 68 per cent of those with IBS were depressed. But this was based on a threshold for diagnosis which was considerably lower than that usually used, and verified, with this questionnaire. This inventory also contains a high proportion of 'somatic' symptoms, as does the Hamilton Depression Rating Scale (HDRS), where 30 per cent of the score is so derived. Using the HDRS Kingham and Dawson (1985) considered 64 per cent of their 22 IBS patients to be depressed. But these patients clearly had severe, refractory symptoms ; indeed they had undergone a total of 38 operations for their abdominal symptoms.

MacDonald and Bouchier (1980) studying consecutive referrals to a medical outpatient clinic, found psychiatric illness in 53 per cent patients where the diagnosis was of functional gastrointestinal disorder, and in 20 per cent in those with an organic gastrointestinal diagnosis. They used a standardised research interview. Craig and Brown (1984) found similar prevalences in a

study of 79 patients with functional bowel disorder. The prevalence of psychiatric illness was 42 per cent in the IBS group compared with 18 per cent in a matched control group with chronic organic gastrointestinal disease, and eight per cent in a community control group. One study has shown conflicting results. Fava and Pavan (1976) reported a higher prevalence of psychiatric illness in the patients with an organic diagnosis.

Of 31 patients described by Hill and Blendis (1967), in 19 the diagnosis was probably essential dyspepsia (there was no bowel disturbance) ; only six of his subjects would meet current IBS diagnostic criteria. He considered six patients to be depressed, five of whom responded well to antidepressants. In such series it is always difficult to establish which symptoms developed first. Liss et al (1973) considered that in 68 per cent of his patients psychological symptoms preceded somatic symptoms, whereas the reverse was true in only eight per cent. Young et al (1976) thought the relative figures were 55 per cent (psychological first) and 25 per cent (somatic first).

Personality.

Esler and Goulston (1973), using the Eysenck Personality Inventory (EPI) and the Institute for Personality and Ability Testing Anxiety-scale Questionnaire, found IBS patients (16, diarrhoeic type) obtained scores similar to patients

with chronic anxiety neuroses over a range of parameters. 15 pain-predominant IBS patients were more introverted, but in other respects similar to the controls drawn from medical outpatients. A group of patients with ulcerative colitis were indistinguishable from the controls. The psychological profile of IBS patients is more disturbed than that of patients with similar reported symptoms, of similar duration, but who have an organic disorder (West 1970).

IBS patients studied by Whitehead et al (1980) using the Hopkins Symptom Checklist (HSC) scored higher on all the global scales than the controls. The 17 patients also had higher scores on five clinical subscales ; somatization of affect, interpersonal sensitivity, depression, anxiety, and hostility. There was no correlation with the severity of gastrointestinal symptoms. Palmer et al (1974), using EPI and Middlesex Hospital Questionnaire (MHQ) (Crown and Crisp 1966), suggested that IBS patients displayed a degree of neurotic personality structure. Their psychoneurotic-symptoms-score fell between that of the normal controls and that of the comparison group with established psychoneurotic disorder.

Welch et al (1984) found IBS patients scored higher on MHQ scales for anxiety, phobic anxiety, and somatisation than normal controls. However the IBS patients were not different from a third group of patients with organic gastrointestinal disorders on these scales, nor on a Zung self-rating

depression scale. The numbers in the study are small, and the organic diagnoses include lymphoma, and colonic and gastric polyps (the group were drawn from patients awaiting endoscopy). Length of history is not stated. It is not clear whether the similarity reflects longstanding similarity in psychological profile or whether the profiles are converging as a consequence of short term, perhaps reversible, changes in one or both groups (one would not be surprised by increased psychological distress in such patients awaiting investigation).

Bergeron and Monto (1985) found 70 per cent of IBS patients had psychopathology as assessed by the MMPI ; but half the patients were volunteers for a stress reduction programme. He considered that there were several patterns of psychological dysequilibria;

1. inadequate dependency, characterised by a chronic pattern of depression.
2. somatization: emotional problems tend to precipitate multiple physical complaints, often with denial, unrealistic optimism, and a resistance to psychological attribution.
3. reactive depression characterised by excessive worry, anger, and denial.

Whitehead et al (1988) found an increase in symptoms of psychologic distress on HSC in IBS patients compared to controls or non-reporters. A

similar pattern emerged comparing lactose malabsorbers seen in clinic with those seen in the community. It seems reasonable to conclude that IBS patients have greater evidence of psychopathology than normal healthy individuals and patients with similar gastrointestinal dysfunction but a specific organic diagnosis.

There is a further possible confounding factor in the assessment of psychological parameters by questionnaire. Schema is a cognitive framework of beliefs, attitudes, and self perception which influences information processing and is stored in the memory. In major depression patients have a higher recall of 'depressed' words. Toner et al (1990) compared IBS patients with patients with major depressive illness. In the IBS subgroup meeting DSM criteria for a diagnosis of depression in the preceding year, there was recollection of a lower proportion of depressed words than in the depressed group. Thus IBS patient have less chance of seeing themselves as depressed. This accords with previous work (Latimer et al 1983) showing higher Lie test scores in IBS patients than in non-patient controls. Such higher scores can reflect ;

1. deliberate faking of answers
2. less candid self assessment
3. less insightful assessment (though no less honest)

It is therefore evident that a substantial proportion of IBS patients meet diagnostic criteria for a variety of psychiatric diagnoses at the time the IBS diagnosis is made, and that on average they are more likely to have evidence of psychological distress or disturbance (even in the absence of a formal psychiatric diagnosis). In assessing the psychological status of IBS patients one must be aware that instruments designed to look for depression in putatively depressed subjects, or to seek psychopathology in normal populations, may be inadequate or misleading given the view(s) IBS patients may hold of their experiences. Despite the acknowledged limitations questionnaires do seem to offer an insight into possible psychopathology, provided they are interpreted with caution and circumspection.

The circumstances in which this interaction is occurring.

The suggestion that stress was a significant factor in IBS appears early in the literature, with war the proposed 'stressor' (Da Costa 1871, Peters and Bargen, 1944). Chaudhary and Truelove (1962) recognised at least one psychosocial factor in 65 per cent of their 130 patients. Here the factors included difficulties with marital, family or business relationships. Marital difficulties were again emphasised by Hislop (1971) in his comparative study of 67 IBS patients and controls. Kirsner (1981) postulated that less dramatic events might also be important ; changing job, moving house, financial problems.

Hislop (1971) further identified 'emotional distress in childhood' as being more common in IBS patients. Childhood deprivation was frequent in a second Hislop (1979) study though this was uncontrolled. Mendeloff et al (1970) found consistently higher scores of life stresses in IBS patients than in patients with ulcerative colitis or subjects from the general population. Death of a close relative was associated with IBS in a controlled study (Gomez and Dally 1977). Both IBS and ulcerative colitis were more frequently preceded by life events in the six months before the onset of symptoms than was appendicitis. Particular event classes were notable exits (death, separation) and undesirable social events (demotion, unemployment) (Fava and Pavan

76/77). Interestingly this group had previously shown no preponderance of life events coinciding with (or preceding) IBS, but the control group here was patients with ulcerative colitis. The importance of loss as a characteristic of life events has been stressed by several authors.

The interaction between life events and symptoms, notably abdominal pain, is further shown in several studies examining the outcome of 'acute appendicitis'; comparing those patients in whom the appendix is histologically normal with those in whom there is histological inflammation. Harding (1962) first emphasised the importance of psychosocial factors in the former group, many of whom may well have IBS. Ingram and Evans (1965) found evidence of psychological disturbance in 83 per cent of women who had a normal appendix removed, but in less than 20 per cent in those with histological appendicitis. Of those with a normal appendix, at least 50 per cent were continuing to have pain one year later, as were 10 per cent of those with an inflamed appendix. The nature of the pain may give some clue as to the true diagnosis. Barraclough (1968) found that continuous pain was more common in those with noninflamed appendices and he confirmed that this group was more anxious. In a study of life events preceding appendicectomy both operation groups scored more highly for life events than a community control group (Creed 1981). But the pattern of events in those with noninflamed appendices more closely resembled that found in depressed patients than did the pattern in inflamed appendix patients. Continuing abdominal pain was a

feature in those with this 'depressive life event profile'.

Craig and Brown (1984) analysed 'stressful life situations' in the year preceding onset of abdominal pain, and found differences between patients with a gastrointestinal clinic diagnosis of organic disease and those with a diagnosis of functional disorder. Again the striking characteristic of the events was that they carried a loss or 'goal frustrating' element and were comparable to those which often precede depression. Although stressful events of certain classes may be particularly powerful, it can be argued that in the development of a life events profile, less dramatic events may assume a powerful cumulative significance.

Ford et al (1987) reported that there was a difference in experience between patients with functional and organic gastrointestinal disease. Anxiety-provoking life events were important only in those with psychiatric illness but 31 per cent of those with a functional diagnosis had experienced psychiatric illness, and 35 per cent had experienced an anxiety provoking situation, prior to the onset of symptoms. He suggested that the interaction between the life event(s) and long established experience might lead to symptom reporting.

Previous exposure to, and experience of, symptoms and illness behaviour

A strong family history of abdominal complaints has been a recognised feature of IBS patients for several decades. Ryle (1928) described a familial tendency in childhood abdominal pain. The prevalence of current functional abdominal complaints was much greater in the families of IBS patients than in controls' families (Davidson and Wasserman 1966, Apley and Naish 1958). Children with chronic abdominal pain often have parents or siblings with similar complaints. But such children do not have parents who suffered from abdominal pain in childhood themselves (Christensen and Mortensen 1975). This suggests that imitative behaviour plays an important role, perhaps as important as any genetic component. Lowman et al (1987) found that IBS patients (and interestingly also non-patients) recalled more frequent childhood doctor visits, more numerous bowel complaints in childhood, and greater parental attention to illness, than did normal controls. Loss and separation during childhood was more common in IBS patients.

For many years IBS was regarded as a chronic relapsing condition ; patients were often perceived as chronic clinic attenders ; there was much therapeutic nihilism which persists in some clinicians today. However IBS patients are not a homogeneous group and the prognosis varies. There are some useful prognostic indicators. As long ago as the 1920s Dawson (1921) wrote that the prognosis was in his experience good if the associated constipation could be cured without resort to colonic irritants. After one to three years 30 per cent of Chaudhary's patients were symptom free (Chaudhary and Truelove 1962). Determinants of symptom improvement included precipitation of the IBS by a dysenteric illness or a preceding major stressful life situation. In most studies length of history is not a useful guide to prognosis. Waller and Misiewicz (1969) commented that '*complaints continued much as before but patients felt so much better that symptoms faded into the background*'. They considered that stress played an important part in 75 per cent of their patients, being the factor which most frequently changed experience into symptoms. One can understand the confusion surrounding prognosis in IBS when this paper is used in support of arguments that the prognosis is 'poor', quoting the low 'symptomatic response rate' of 12 per cent (Nanda et al 1989).

40 per cent of patients were symptom free up to 20 years after presentation

with 'functional diarrhoea' (in half abdominal pain was also a feature). One fifth were still experiencing persistent symptoms. An alternative diagnosis had emerged in only three patients (Hawkins and Cockell 1971). Holmes and Salter (1982) found four alternative diagnoses in their 77 patients ; gastric ulcer, jejunal diverticulae, hyperthyroidism, and hypothyroidism. 44 per cent of the patients had persisting symptoms six years after initial diagnosis.

Surprisingly Hastrup Svendsen et al (1985) found one case of pancreatic cancer and one of chronic pancreatitis in a 129 patient series. In a five year retrospective analysis 50 per cent of patients reported unchanged or worse symptoms independent of treatment. Abdominal surgery before diagnosis was an indicator of poor symptom control. In a five year prospective study Harvey et al (1987) found 68 per cent of patients became virtually symptom free. Good prognostic factors were male sex, predominant constipation, short history, and symptoms following a diarrhoeic episode.

Misra et al (1989) studied the relapse rate in 28 patients who had previously improved on treatment with ispaghula husk and propantheline when such treatment ceased. They found symptomatic relapse rates of 82% and 46% in the placebo and continuing treatment groups respectively. All their patients had 'recovered completely' after four to six weeks treatment and the group is certainly not typical of IBS sufferers. No mention is made of initial fibre intake.

The relapsing nature of IBS and the unknown pathophysiology render clinical treatment trials difficult. Outcome measures are difficult to define and have tended to rely on sequential symptom reporting or assessments of 'general wellbeing'. Generalisation from trials is often difficult because symptoms are not well defined and the psychological profile of the patients is often not considered.

Antispasmodic agents

Given the lack of a specific association between symptoms and motility and of a unique motility disturbance, it is not surprising that antispasmodic preparations have a limited efficacy in IBS. In the following discussion only trials with a placebo control arm are considered since without this interpretation is impossible.

Phenytoin (Greenbaum et al 1973) is known to reduce smooth muscle contraction but in 12 patients treated for 20 weeks in a double blind crossover trial there was no advantage over placebo in improvement of IBS symptoms.

Trimebutine was more efficacious than placebo in a double blind crossover study. However the treatment duration was only three days and the placebo

response rate was remarkably low at five per cent (Luttecke 1978). The advantage over placebo was not repeated in a second study from the same author (Luttecke 1980). Fielding (1981) demonstrated no advantage over placebo in 60 patients treated for six months.

Mebeverine has been variably reported to be useful in IBS. Bertholet and Centonze (1981) in an 8 week study period claimed advantage over placebo, though the placebo response rate was 73 per cent, and his 69 patients were rather older than on most IBS series (mean age 57 years). Kruis et al (1986) could not demonstrate advantage over placebo in 70 patients treated for four months.

Dicyclomine was claimed to affect a response in 94 per cent of 97 patients treated for two weeks (Page and Dirnberger 1981).

Peppermint oil has been used in three trials of up to three weeks treatment duration. Two trials claimed benefit with response rates of 80 per cent (Dew et al 1984, Rees et al 1979). The third showed no advantage over placebo (Nash et al 1986).

Loperamide is an opioid which increases small intestinal transit time and may decrease urgency or borborygmi. In 28 patients who had not responded to bran there was a favourable response to loperamide but this was also true

for placebo. Only diarrhoea and urgency showed a clinical and statistical response greater with loperamide (Cann et al 1984a). Hovdenack (1987) claimed a response rate of 100 per cent in 60 patients treated for three weeks. The patients are not well described and this result simply does not accord with general clinical experience.

Domperidone, a prokinetic agent which reduces transit time, was disappointing in two studies of four and twelve weeks duration. (Cann et al 1983a, Fielding 1982) A third study reported beneficial effect after four weeks, but here again the response rate is said to be 100 per cent (Milo 1980).

Calcium antagonists may ameliorate exaggerated colonic motility response to food (Narducci at al 1985, Prior et al 1987) but this has not yet been reflected in clinical usefulness. Nifedipine gave disappointing results in 20 patients treated for three weeks (Perez Mateo et al 1986).

In 80 patients also given 30g fibre daily the response rate with Timolol over a six month follow up period did not differ from the placebo response rate. There was improvement in abdominal pain and doctors' general assessment in 65 per cent of both groups (Fielding 1981).

Many studies examining the effect of fibre supplements are flawed by poor quantification of baseline fibre intake, the lack of a control group, and insufficient characterisation of the dietary fibre supplement. Such trials are often short term.

Prior and Whorwell (1987) describe 80 patients treated for 12 weeks with ispaghula. 82 per cent of the active and 53 per cent of the placebo group were globally improved but this seemed to reflect reduced constipation ; abdominal pain and bloating were not changed. Kumar et al (1987) showed that symptom score improved with daily supplementation of 10g, 20g, and 30g of ispaghula husk in 14 male patients after 17 days. There was a significant increase in stool weight, most marked with 20g and 30g daily supplements. Whole gut transit time remained relatively constant. Fielding and Melvin (1979) described how an increase in dietary fibre intake caused improvement in symptoms. In this study those patients who did not improve were those whose fibre intake had not increased despite dietary advice. Manning et al (1977) studied 14 patients who received a daily supplement of 20g cereal fibre for six weeks. The study was not blinded. Symptoms were improved and there was an associated change in colonic myoelectric activity.

However studies which have demonstrated little or no effect of fibre are in the majority and the concensus view is that while fibre supplement may reduce constipation it has little effect on the other complaints which comprise the IBS symptom complex.

Hillman et al (1984) followed 30 IBS patients for up to three years. Initial fibre intake correlated poorly with symptoms and bowel habit. Half the patients were improved by a mean increase in daily fibre intake of 6.7 g/day. There was no difference between this and the placebo group. No clinical score predicted individual course. Soltoft et al (1976) described a placebo controlled double-blind trial of 59 patients. The active group received 30g bran daily without significant symptomatic response after six weeks. Baseline fibre intake was not given. In a double blind trial involving 77 patients there was no difference in response between the placebo group and that taking a vegetable fibre supplement over 12 weeks (Longstreth et al 1981).

Arthurs and Fielding (1983) found no difference from placebo in 80 patients after four weeks using ispaghula ; active and placebo response rates were both of the order of 70 per cent. Cann et al (1984b) studied 38 patients in a non-blind, controlled study over four weeks. 47 per cent of active treatment subjects considered themselves improved on 10-30g wheat bran supplement daily ; not significantly different from the placebo subjects. Bran did reduce constipation. Lucey et al (1987) achieved response rates of approximately 75

per cent in treatment and control groups with wheat bran supplements for 12 weeks.

Arffmann et al (1986) showed increased stool weight but no effect on symptoms compared to placebo in 20 patients taking a 30g supplement of wheat bran for six weeks. There is insufficient detail in the paper to allow assessment of the placebo response.

Antidepressants

From the prevalence of depressive symptoms and possible depressive illness in IBS patients, one would anticipate that antidepressants would be efficacious in a substantial proportion of such patients. However the use of antidepressants in IBS remains contentious. Where a diagnosis of depression is made there is a clear place for consideration of antidepressant therapy. But in those patients not thought to be suffering form a depressive illness antidepressants may still be advocated. Of course tricyclic antidepressants have anticholinergic effects but peripheral anticholinergics have yielded disapppointing results in IBS. Those patients who do respond may have an unrecognised depression.

Further difficulties are raised by the time course of the improvement in those studies where there is benefit ; symptomatic response occurs long before a mood lifting effect would be expected, often within the first ten days of treatment (Hislop 1971, Heefner et al 1978, Myren et al 1982, Steinhart et al 1981). It is interesting to note the similarity here with emotionalism after brain injury, notably after acute stroke which likewise responds variably to antidepressant medication and often within 72 hours. There are no double-blind controlled trials of longer than eight weeks of antidepressants in IBS and in the shorter trials the outcome measures, and the duration and

characterisation of symptoms, is poorly defined. It is not possible to make a firm judgement on the efficacy of antidepressant treatment in IBS.

Combination treatments also have advocates. Ritchie and Truelove (1979) used varying combinations of hyoscine (an anticholinergic antispasmodic), lorazepam (a benzodiazepine), and fybogel. 38 per cent of 98 patients improved over three months. None of their placebo patients improved and they concluded that there was little benefit from placebo in IBS. In a subsequent non-placebo trial similar improvements were shown with mebeverine, fluphenazine and nortryptiline, and bran (approx 20g daily). The combination of all three was most powerful. Although the authors comment that lorazepam was not more efficacious in those with high anxiety scores, nor fluphenazine and nortriptyline in those with high depression scores, the figures on which these interpretations are made are not given (Ritchie and Truelove 1980). Lancaster-Smith (1982) claimed benefit from a fluphenazine and nortriptyline combination, although only one of eight examined parameters was improved.

Upto 10 one hour sessions of individual psychotherapy caused reductions in symptoms at three and twelve months in a controllled trial of 101 outpatients (Svedlund 1983). Schonecke and Schuffel (1975) had previously shown no such improvement in a shorter term study. Hislop (1980) found psychotherapy of benefit in 60 patients followed up for two years. Whorwell et al (1984) found hypnotherapy highly effective in 30 patients with severe refractory IBS (mean of six previous treatments) after seven half-hour sessions over three months. There was no deterioration after 18 months. The placebo group, who received supportive psychotherapy, also improved, but to a significantly lesser degree. The support comprised explanation and discussion of symptoms and of emotional problems.

Disturbing thoughts are common in normal people and often relate to health worries. Such thoughts and their interaction with experiences may prompt the sufferer to seek 'reassurance'. Although the reassurance may reduce short term anxiety, the nature of the process of reassurance may serve to increase the perceived validity of the distress and thereby increase longer term disturbance. This may provoke further reassurance seeking and a vicious cycle is established (Warwick and Salkovskis 1985). Systematic prevention of this reassurance-seeking behaviour has been developed in the management of obsessional states and perhaps the technique is applicable in IBS.

Certainly repeated investigations often serve simply to confirm the IBS patient in the view that 'there must be something wrong' (Kreitman et al 1965). Reassurance must be appropriate and directed, and the reassurer should be as aware of the emotional concerns of the patient as of their physical symptoms.

Cohen and Reed (1968) described how 'nervous diarrhoea' was improved by a desensitisation programme. This experience is of limited relevance since the 'nervous diarhoea' discussed occurred in only two of the six described cases, and was characterised by frequency of defaecation precipitated by travelling. The subjects would not fulfill most criteria for a diagnosis of IBS.

Illness behaviour theory does seem to be a valid framework within which to construct a model of IBS. Pilowsky first described the concept of abnormal illness behaviour and has subsequently described the necessary characteristics ;

> *'the persistence of an inappropriate or maladaptive mode of perceiving, evaluating, and acting in relation to ones own state of health, this despite being offered (by the doctor) an accurate, reasonable, and lucid explanation of the illness, its nature and its treatment, with opportunities for discussion, clarification, and negotiation based on an adequate assessment of all biological, psychological, and social factors.'*
>
> (Pilowsky 1969)

Behaviour theory suggests that rewarded behavioural patterns will be repeated or copied. It is known that learning can influence gastrointestinal functions such as gastric acid secretion or colonic motility, particularly if feedback loops are employed (Miller 1977). The development of a chronic illness behaviour profile is facilitated by rewarding illness behaviour. This facilitation may be particularly important in childhood.

Based on insights such as these and on the features of IBS, Latimer (1981) has proposed a behavioural model for IBS. This model rests on three major propositions ;

1. That events, symptoms, and behaviours are independant variables. The same physical stimuli can produce different behavioural responses, motor and emotional, in the same individual as well as in diverse individuals (Schachter and Singer 1962). It is counterproductive to attempt to place the event, any subsequent reported symptoms, and any consequent behaviour on a single linear axis since the confounding inputs from factors other than the initiating 'event' play such a powerful role in shaping the overall response.
2. IBS is a a continuous disorder with no clear demarcation from normal experience. There is no single characteristic which sets the IBS patient apart.
3. There is a familial predisposition to certain kinds of behavioural response. These patterns may be regarded as unlearned and unadaptive. The behaviour patterns observed in IBS may originate in such unlearned response patterns.

This behavioural model can be usefully refined by integrating aspects of the phenomena of somatisation and amplification.

Amplification is described as the consequence of a heightened attention focus on bodily sensations, and / or a tendency to select out and concentrate on certain relatively weak and infrequent sensations (Barsky et al 1988). It may be accompanied by a disposition to react to such sensations with an affect and cognitive process which intensifies them and makes them alarming, ominous, and disturbing (Barsky 1979). A disposition to respond in a certain way is a personality trait, a persisting characteristic. The trait termed neuroticism is particularly noteworthy in his discussion. The tendency to report and experience a wide range of negative emotions, neuroticism is a reliable, valid and stable construct with associations with introspection and a tendency to depressive symptomatology (Watson and Clark 1984). It can be argued that the degree to which traits are expressed at a given time is influenced by emotional state.

These concepts have much in common with those used to describe somatisation. This has been defined as ;

> *'an idiom of distress in which patients with psychosocial and emotional problems articulate their distress primarily through physical symptomatology'*
>
> (Katon et al 1984).

The behavioural aspects were subsequently emphasised ;

'the expression of personal and social distress in an idiom of bodily complaints with medical helpseeking'

(Kleinman and Kleinman 1985).

Somatoform disorders have been divided into four classes;

1. In conversion states the major dysfunction is in behaviour. Ideation and communication may be unaffected.
2. In hypochondriasis, behaviour is often least affected, the disruption being principally one of ideation and communication.
3. Somatiform pain is also characterised by abnormal ideation and communication with relatively little behavioural disturbance.
4. Somatisation is distinguished by elements of dysfunction in all three domains; ideation, communication and behaviour.

Somatoform disorder need not be diagnostic category and Goldberg has emphasised that somatisation does not imply psychiatric illness (Goldberg 1979). However somatic presentation is extremely common in depressive illness ; the majority of patients with psychiatric illness do not present with psychological compliants, but with physical symptoms alone (Goldberg 1979, Bridges and Goldberg 1985). The consulting behaviour of such patients is determined by their attribution of the symptoms to a physical disorder and they seek help for the somatic manifestations only.

Using these insights IBS symptom presentation may be conceptualised as originating in an unlearned, maladaptive response which may be consolidated into personality structure. This response will be manifest in behaviour only when external or internal events are perceived as sufficiently threatening to evoke the response. The threshold for this response may vary according to the emotional state and mood of the individual and the response itself may be influenced by adaptive learning, by which the response is altered to better effect amelioration of the disruption caused by the events.

Elements of the maladaptive response may persist because of advantages they confer.

1. The help-seeking behaviour may increase social interaction which may of itself be sufficient reinforcement. These motives are of course dominant themes in Balint's theories (Balint 1957).
2. Somewhat paradoxically the mood disorder, particularly depression, may be reduced by somatisation. The maladaptive response may permit avoidance of responsibility or blame (Goldberg and Bridges 1988).
3. This may be the only method of distress-communication available to the individual, or may be the only language of such distress-communication which is socially accepted. This sociocultural influence may be particularly important ; somatisation is the norm in most of the worlds' cultures.

Several important differences have indeed been noted between somatisers and non-somatisers in studies of depressive illness. The psychiatric disorder tends to be more longstanding in somatisers, and marraige relationships tend to be poorer. Interestingly, however, there tends to be less disruption of social, family, and occupational networks, and less anxiety, in those patients who somatise their distress (Goldberg and Bridges 1988).

But somatisation has disadvantages too, though they may not be perceived, or indeed perceivable, from the patients perspective. Psychiatric disorder may not be recognised, diagnosed and treated. Inappropriate investigations may be ordered, and iatrogenic disease needlessly precipitated. Abnormal illness behaviour patterns may become established. Kirsner (1981) proposes that IBS can be regarded as a negative interaction with medical systems.

These observations may have implications for the management of IBS. Abolishing symptoms may not be an appropriate objective where they arise as an unlearned coping response. Rather it may be more rational and fruitful to seek to influence the mechanisms by which the response is refined and the behaviour determined, accepting that at times the response (the symptom complex) is likely to recurr.

Goldberg describes four stages in this process of reattribution ;

1. assessment.
2. changing the agenda, focussing away from the somatic complaints.
3. encouraging recognition of the link between the somatic symptoms and the psychic distress.
4. development of a coping strategy for recurrence of the response.

This does not necessarily require patient insight into the pathogenesis of the maladaptive response, but it does require that the consulted physician be alert to the possible psychological determinants of somatic presentations. Some general practitioners seem to produce more somatisation than others, though this may reflect prior selection of patients with the propensity to so react, rather than the general practitioner influencing the reaction per se. The behaviour and future response of the IBS patient will be forged in the conduct of the doctor-patient relationship.

However the conceptual framework of somatisation tends to perpetuate the duality of emotional and physical disorders. A more useful approach may be to consider emotional and motor responses as part of the totality of behaviour (Weiner 1989). All behavioural acts (emotional and motor) can be seen as neurally mediated responses which occur in relation to the conditions under which they occur (ie behaviour, voluntary and reflex, is intrinsically conditional).

It follows that adaptability (and maladaption) is likewise conditional. It is, after all, accepted that associative conditioning can influence behaviour (ie stimuli can be recognised), and that operant conditioning can reproduce the reflex behaviour under different conditions.

From the illness behaviour model and the observations regarding IBS which I have considered, there developed a model of IBS based on the proposition that the symptom complex and medical-help-seeking behaviour were the product of an interaction between three influencial domains ; soma, psyche, and circumstance. These could be represented as apices of a triangle (Ford et al 1982). The studies described here examine elements of this model and the thesis suggests refinements of this behavioural approach which may allow greater insight into the development, natural history, and treatment of IBS.

AIMS

To assess the correlation between gastrointestinal symptoms and general well-being in IBS.

To investigate whether a fibre supplement given as tablets will influence gastrointestinal symptoms or general well-being in patients with IBS.

To assess the placebo response in patients with IBS.

To register psychopathological variables in order to investigate possible correlation between psychopathology, irritable bowel syndrome, and the putative therapeutic effect of dietary fibre.

To investigate the correlation between questionnaire and visual analogue scale assessments of anxiety and depression in patients with irritable bowel syndrome.

To measure salivary IgA concentration in IBS patients and investigate any correlation between this and psychopathology or treatment response.

To consider whether alcohol plays a part in the aetiology of the IBS symptom complex.

To assess the possible usefulness of platelet serotonin and urinary metanephrine as biochemical indicators of psychopathological variables in IBS.

To examine the 5 year prognosis of IBS and consider psychopathological influences on the 5 year outcome.

To consider the impact of attendance at a specialist GI clinic on the GP attending behaviour of IBS patients.

STATISTICAL METHODS

Statistical advice was obtained from the Department of Medical Statistics of The University of Edinburgh. As a result of this advice Student's t-Test was used to compare mean levels between groups of patients, because of its robustness to departures from normality of distribution with reasonable sample sizes. In the tabulated results mean values and standard deviations (SD) are accompanied by the range. Where the distributional assumption is threatened and variances do not permit the use of parametric tests, appropriate nonparametric Mann Whitney U test is used to compare groups.

Analysis of association between pairs of variables was by Spearman coefficient of rank correlation (R) to avoid distributional assumptions. The product-moment correlation coefficient (r) is also given where appropriate in recognition of its greater sensitivity and reliability.

Analysis of the treatment trial was on an 'intention to treat' basis, using the last available data from patients who withdrew after the 4 week symptomatic assessment.

THERAPEUTIC TRIAL

Recruitment

Subjects were recruited from the outpatient clinic of a specialist Gastrointestinal Unit. All had been referred by their general practitioner. The patients were asked to consider participating in the therapeutic trial after the diagnosis of IBS had been established in the outpatient clinic. This would usually take one or, less frequently, two visits. No medications were given or dietary advice offered at this stage. Patients were recruited predominantly from the clinic of one consultant gastroenterologist, though the units' other two gastroenterology consultants referred some patients. 49 suitable patients were identified and recruited over a 9 month period. Patients were all approached by the investigator in the clinic and gave informed consent in accord with the Helsinki declaration II. The study was approved by the local ethical committee.

Diagnostic Criteria

The diagnosis of irritable bowel syndrome was made on the basis of the following features :

1. an altered bowel habit of at least 6 months duration unaccompanied by rectal bleeding
2. the presence most days of abdominal pain
3. relief of pain with defaecation
4. abdominal distension.

Only those in whom the altered bowel habit was constipation (straining to pass hard stool less than 3 times a week) or alternating frequent defaecation and constipation (as defined above) were included. The diagnosis was not sustainable in the presence of features of systemic disorder particularly weight loss, sweats, or eye or joint symptoms.

All subjects had normal general, abdominal and sigmoidoscopic examinations. Rectal biopsies were taken in 42 cases; all were normal. In all subjects full blood count, erythrocyte sedimentation rate (ESR), urea and electrolytes, and thyroid function tests were within the laboratory's normal reference range. Double contrast barium enema was normal in the 48 cases in which it was obtained.

Exclusion criteria

All subjects were outpatients with a diagnosis of IBS as defined above, aged between 18 and 80 years. The following were grounds for exclusion :

Irritable bowel syndrome with diarrhoea as the predominant bowel habit without periods of constipation.

Patients currently using fibre supplements, or in whom such supplementation had previously been used as a sustained treatment for their symptoms.

Use of the following medications ; laxatives, anticholinergic agents, drugs with anticholinergic activity, opioids with constipating effect, H2 blockers, ganglionic blocking drugs.

Patients with a concomitant or previous diagnosis of anxiety neurosis or depression were excluded, as were those in whom specific psychotropic medication was being taken or was thought necessary by the clinic physician or investigator.

Exclusion criteria

The presence of other diseases of the gastrointestinal tract or of colonic diverticula on barium enema.

Significant indigestion.

Endocrine disease including myxoedema.

Pregnancy.

Trial Design : a double-blind, placebo-controlled, randomized trial.

Subjects were randomised to receive either concentrated fibre or placebo tablets. Randomisation was by the supplier of the tablets, based on random number tables which designated the trial number active or placebo. The binary code was not revealed to the investigator until after the clinical trial was finished, and the identity of active and placebo groups was revealed only after statistical analysis was complete. The fibre tablet contained a mixture of cereal and fruit fibre; 44% of its 624 mg was analysed and measured as dietary fibre. The placebo, a mixture of starch, calcium phosphate, and lactose had a dietary fibre content of 29 mg and looked identical to the active tablet. All subjects were instructed to take 5 tablets 3 times daily, at mealtimes, accompanied by a large glass of water. Subjects in the concentrated fibre tablet group received a daily supplement of 4.1 g dietary fibre, those in the placebo tablet group 0.4 g.

A one-week run-in period (week 0) was followed immediately by a 12 week test treatment period. Symptom assessments were performed at the start of weeks 0 and 1, and at the end of weeks 4 and 12. The daily dose of test tablets was estimated by the patient ; this assessment of compliance was coupled with a request to return any unused tablets.

Possible side-effects and concomitant medication were also recorded. At the end of test treatment a subjective evaluation of the effect of the treatment was also sought.

Symptom assessment : gastrointestinal symptoms

At the recruitment visit subjects were asked about specific gastrointestinal symptoms. In the week before treatment was started (week 0), the subjects completed a seven day diary of daily bowel movements, type of stool and the occurrence of abdominal pain. [Appendix 1] The week-long diaries were completed again during weeks 4 and 12. From the diary three scores were calculated :

1. pain score

   The sum of each daily recording 0 (absent), 1 (slight), 2 (moderate), 3 (severe). Where more than one entry was made in a single day the highest was used for that day in the summation.

2. frequency score

   The number of stools in the week.

3. constipation score

   The consistency of each stool was recorded as follows ;

   hard or broken (1), pellety (2), normal (3), soft (4), watery (5).

The constipation score was calculated as the sum of the daily (number of stools x consistency). The lower this score, the less frequent and harder the stool.

A single investigator interviewed all subjects at recruitment and at the end of weeks 0, 4 and 12, recording the parameters shown below.

Symptom	Score
urgency to defaecation	yes (1) / no (0)
constipation	0-3
abdominal pain	0-3
relief of pain at defaecation	yes (1) / no (0)
mucous in stool	yes (1) / no (0)
abdominal distension or bloating	0-3
flatulence or borborygmi	0-3
sensation of incomplete evacuation	yes (1) / no (0)

The total score (maximum 16) was taken to represent the global symptom score.

Symptom assessment : general evaluation of well-being.

Each subject was asked at the end of the study if they felt 'generally better', 'unchanged', or 'worse' for having taken the tablets.

Assessment of fibre intake

Between recruitment and the start of week 0 each patient was interviewed by a single dietician. A 24 hour recall evaluation of carbohydrate, fat, protein, alcohol and dietary fibre intake was obtained. The dietician was unaware of symptom severity or character, and offered no dietary or other treatment advice. Daily dietary fibre intake was calculated using data from McCance and Widdowson's the composition of foods (Paul and Southgate 1978).

There are several approaches to the assessment of dietary intake. I was particularly interested in dietary fibre intake and in comparing groups of subjects. The 24 hour recall method was chosen because of its ease of administration and validity in group comparisons. The subject is asked to recall their exact intake for the preceding 24 hours. Recent memory may be more accurate, particularly for quantity, than a general diet history approach. Although there is significant under-reporting of intake by this method, analysis of variance demonstrates good correlation between actual and recalled values (Madden et al 1976).

But individuals diets' vary from day to day. Comparing a single 24 hour recall assessment with the daily average from a seven day diary, Young et al (1952)

found very close correlation for nutrient divisions; indeed the group means were 'interchangeable'.

However, self-recording may influence such results and most studies show significant day to day variations in the 24 hour recall profile of individuals (Balogh et al 1971, Heady 1961). However these disadvantages need not invalidate 24 hour recall as a method for assessing and comparing the dietary profiles of groups of subjects. There is considerably less day to day variation in the mean intake of groups of subjects. Heady (1961) and Hankin et al (1967), in groups of 116 and 93 subjects, confirmed large day to day individual variation, but demonstrated stability of the group mean. Thus, although 24 hour recall is not a valid tool for assessing individual intake, it has considerable support as a means of assessing dietary profiles of groups of subjects.

Assessment of anxiety and depression

1. The Delusions-Symptoms-States Inventory (DSSI)

At the recruitment visit subjects were asked to complete a single-page, 14 item questionnaire examining anxiety and depression based on the Delusions-Symptoms-States Inventory (DSSI) of Foulds and Bedford. [Appendix 2] The DSSI was developed as a self report measure which would facilitate classification of psychiatric illness (Foulds and Bedford 1975). The inventory includes assessments of 'states of emotional disturbance', which comprise the first and lowest class (Class 1) in the four class hierarchical model. Depression and anxiety are two of the three dysthymic states in Class 1. The states are more descriptive than diagnostic - an individual falling into one of these states might be said to be 'emotionally stirred up'. It might be said that most individuals experience these states at some time. It is perhaps easier to see an association between circumstances and these states, than between events and the factors which make up the higher classes.

Each class in the hierarchical model (Class 2 [symptoms], Class 3 [delusions], and Class 4 [disintegration]) comprises several sets examining a range of emotional phenomena and psychiatric symptomatology. Each set

has seven items, for each of which the response scores 0 - 3. The maximum response is therefore 21 for each of depression and anxiety. It was decided arbitrarily during formulation of the inventory that a score of 4 or more should indicate true states/symptoms within the sets. The DSSI has been validated in psychiatric patients and in normal UK subjects (Foulds and Bedford 1975).

2. Visual analogue scales

A line rating visual analogue scale (VAS) was explained and an example illustrated and completed. [Appendix 3] The VAS is expressed in mm, measured from the zero point which represents the minimum available expression of anxiety or depression. 100mm is the maximum score. Measurement of the VAS score was blind to all other assessments of symptoms. Visual analogue scales have been validated as an instrument for assessing aspects of mental state, particularly anxiety or depression (Ingham 1965, Ingham and Miller 1976).

The subjects completed the VAS line rating and questionnaire exercises in private although the same investigator throughout asked about any difficulties before the record was collected.

3. Critique

Personality attributes and emotions, such as depression and anxiety, are difficult to define, to differentiate, and to quantify. Clinical impression is not a satisfactory basis for their study. A reproducible, valid system of assessment is required. To this end many questionnaires have been devised. A frequent drawback of these instruments for examining psychological variables is that they fail to differentiate between personality traits and symptoms (Foulds 1965). If the purpose is to examine severity of an illness or to gain diagnostically significant information, symptoms and signs of illness should be sought in the questionnaire. However if one is seeking to explore relatively enduring personality attributes, the questionnaire must seek to reveal personality traits.

One has to recognise the limitations inherent in the use of questionnaires.

(1) The reliability of the informant (usually the patient) may vary, and their assessment or account may not equate with that of an observer. This is perhaps best demonstrated by obsessional traits which the patient may not recognise (or report) as extreme behaviour or emotion, but which most observers would regard as extreme.

(2) The subject may be reluctant to reveal personal feelings; 'defensiveness'. This may be accompanied by a pattern of response characterised by a greater willingness to acknowledge physical or somatic symptoms than 'psychological' complaints. (Walton and Mather 1962).

(3) Spurious agreement is a confounding overeagerness to admit symptoms - the opposite of 'defensiveness'.

(4) Answers may be influenced by the social desirability of the response (Edwards 1953).

(5) Subjects may, in general, acknowledge extremes of behaviour or emotion (end-users), or may tend to seek to place their experience in the middle ground (middle-users).

(6) Positional bias in responses can arise from the spatial arrangement of the questions and possible responses.

(7) Scoring on multiple response questions gives rise to further unique difficulties as a consequence of 'conceptual distance' (Goldberg 1972). For the respondent the difference between, for example, never and very infrequently may be much greater than that between very infrequently and frequently. But they are presented as though the distance was the same. Goldberg calls this a 'between column problem'. We further assume that the distance between given 'points' on one question is of equal significance to the distance between 'points' on another ; a

'between row problem'.

(8) Linear (graphic) rating scales (Guildford 1954) allow greater freedom of response but the above limitations still apply. One partial solution is to use a 'thermometer scale', defining only the two extremes (for example - never & constantly).

Meites et al (1980) highlight the difficulties in defining and measuring emotions, particularly depression and anxiety. There was considerable overlap between depression and anxiety in a comparison of the Beck Depression Inventory, the Zung Self Rating Depression Scale (ZSDS), the Taylor Manifest Anxiety Scale, and the Neuroticism component of the Eysenk Personality Inventory.

There are difficulties too in differentiating the intensity, frequency, and duration of emotions. This is particularly important when attempting to delineate the relationship between somatic complaints and such psychological variables. ZSDS identified 30% of depressed patients in medical outpatients but missed those patients whose depression presented as a somatic illness. Such scales clearly measure a degree of 'emotionality' but they may not detect a specific state. While this limits the use of such scales in a diagnostic role, it may not be a critical disadvantage in therapeutic terms since the 'emotionality' may respond to treatment, whatever its basis. Nor need it be a critical hindrance in the exploration of a possible aetiological role for emotional factors in conditions which present with predominantly physical symptoms.

However these limitations do have important implications for research, not least in rendering all but impossible the comparison of groups assessed using different methods. Moreover the relationship between somatic symptoms and emotion is not static. The temporal relationship between the onset and severity of the symptoms and emotions may be crucial, but this interrelationship is often difficult to disentangle, particularly in retrospective studies.

Subject characteristics

The age range and sex ratio are similar to most series of irritable bowel patients in the literature [Table 1]. The daily dietary fibre intake is likewise similar to that in the population from which the patients are drawn (Eastwood et al 1984). These patients are certainly not notable for a diet particularly lacking in dietary fibre. Pretreatment dietary fibre intake correlated with reduced constipation [Table 3].

Table 1. *Subjects : Initial characteristics*

	mean	SD	range	median
age (years)	39	13	18 - 76	39
sex ratio (male:female)	17 : 32			
daily fibre intake (g)	20.2	6.1	7 - 31	20
symptom duration (months)	45.8	44.8	3 - 240	12
pain score	6.1	5.1	0 - 17	6
frequency score	10.7	7.3	2 - 30	8
constipation score	33.8	30.2	3 - 141	25
global symptom score	7.3	2.4	2 - 12	8

Table 2. *Association between duration of symptoms and initial symptom scores.*

	r	R
pain score	0.07	0.01
frequency score	0.29	0.23
constipation score	0.18	0.16
global symptom score	0.19	0.16

not significant

Table 3. *Association between fibre intake and initial symptom scores.*

	r	R
pain score	-0.18	-0.09
frequency score	0.23	0.40 *
constipation score	0.26	0.40 *
global symptom score	0.12	-0.07

* $p < 0.05$

Psychometric assessment

The patients found little difficulty in completing the visual analogue assessments of depression and anxiety. They seemed a little more defensive about the questionnaire and this certainly took considerably longer for most patients to complete. Despite this the psychometric tests took less than 10 minutes to administer in the vast majority of patients, none of whom were unwilling to complete the assessment. There was a correlation between the questionnaire and visual analogue scales (VAS) measures for both anxiety and depression [Table 4].

There was no significant correlation between the levels of anxiety or depression and the duration of symptoms [Tables 5,6].

The only significant correlation between symptom severity and the psychological tests was between initial pain score and depression line rating score, a further illustration of the relationship between perception and reporting of pain, and psychological parameters [Table 6].

Table 4. *Assessments of anxiety and depression. (n = 49)*

	Anxiety	Depression
Questionnaire (positive responses)		
mean	1.8	1.1
SD	1.7	1.1
range	0 - 7	0 - 5
Visual Analogue Scale (mm from zero end)		
mean	39	30
SD	16	14
range	11 - 89	4 - 70
Correlation		
r (product-moment coefficient)	0.64***	0.73***
R (Spearman rank coefficient)	0.52***	0.51***

*** $p < 0.001$

Table 5. *Association between anxiety and initial symptom scores. (n = 49)*

	VAS		Questionnaire	
	r	R	r	R
pain score	0.17	0.10	0.20	0.15
frequency score	-0.04	-0.07	-0.21	-0.27
constipation score	0.01	0.04	0.20	-0.19
global symptom score	-0.02	-0.11	0.09	-0.10
duration of symptoms	0.09	0.13	0.03	-0.01

not significant

Table 6. *Association between depression and initial symptom scores. (n = 49)*

	VAS		Questionnaire	
	r	R	r	R
pain score	0.30 *	0.24	0.34 *	0.32 *
frequency score	-0.03	-0.06	-0.05	-0.09
constipation score	0.01	-0.10	-0.01	-0.08
global symptom score	0.06	0.10	0.05	0.05
duration of symptoms	0.11	0.16	0.05	-0.03

* $p < 0.05$

The changes in objective symptom scores are (in general) greatest in those patients with the highest initial scores [Tables 7 - 10]. This may again be a return to the mean phenomenon, although less fastidious recording of bowel habit or altered perception of stool consistency might also have contributed. The change might also reflect an association between perceived symptom severity and propensity to respond to 'treatment'. In this regard it is notable that the global score does not follow this trend. Perhaps this more complicated assessment is less directly susceptible to the interaction between symptom (experience) perception and response to consultation.

Table 7. *Association between the change in pain score and initial parameters. (n = 49)*

	r	R
Symptom duration	-0.26	-0.22
Fibre intake	-0.20	-0.04
Initial pain score	0.41 **	0.31 *
Initial frequency score	-0.14	-0.14
Initial constipation score	-0.18	-0.20
Initial global score	0.17	0.07
Anxiety		
VAS	0.05	-0.02
Questionnaire	0.07	-0.01
Depression		
VAS	0.08	0.01
Questionnaire	-0.06	-0.05

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

** $p < 0.01$
* $p < 0.05$

Table 8. *Association between the change in frequency score and initial parameters. (n = 49)*

	r	R
Symptom duration	0.10	0.09
Fibre intake	-0.05	-0.03
Initial pain score	0.05	-0.06
Initial frequency score	0.67 ***	0.54 ***
Initial constipation score	0.54 ***	0.44 **
Initial global score	-0.20	-0.31
Anxiety		
VAS	0.01	-0.02
Questionnaire	-0.14	-0.07
Depression		
VAS	-0.02	0.02
Questionnaire	-0.10	-0.15

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

*** $p < 0.001$
** $p < 0.01$

Table 9. *Association between the change in constipation score and initial parameters. (n = 49)*

	r	R
Symptom duration	0.14	0.09
Fibre intake	0.05	0.07
Initial pain score	-0.12	-0.15
Initial frequency score	0.60 ***	0.48 **
Initial constipation score	0.67 ***	0.63 ***
Initial global score	-0.20	-0.34 *
Anxiety		
VAS	0.12	0.13
Questionnaire	-0.07	0.03
Depression		
VAS	-0.05	0.00
Questionnaire	-0.08	-0.13

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

*** $p < 0.001$
** $p < 0.01$
* $p < 0.05$

Table 10. *Association between the change in global score and initial parameters. (n = 49)*

	r	R
Symptom duration	0.11	0.00
Fibre intake	0.01	-0.02
Initial pain score	-0.23	-0.20
Initial frequency score	-0.13	-0.02
Initial constipation score	-0.12	-0.06
Initial global score	0.30	0.27
Anxiety		
VAS	-0.24	-0.14
Questionnaire	-0.24	-0.18
Depression		
VAS	-0.21	-0.15
Questionnaire	-0.27	-0.17

r = product-moment correlation coefficient not significant
R = Spearman coefficient of rank correlation

Assessment of outcome

For the purposes of the subsequent analysis the 28 subjects who reported 'improvement' make up one group. The 15 subjects who reported either no change in symptoms at the end of the study (8), or withdrew because of poor symptom response (4) or exacerbation of symptoms (3), constitute the other group, designated not improved.

After three months the outcome whether measured objectively or by overall subjective evaluation, was independant of symptom duration and initial symptom scores [Table 11].

There was a significantly greater reduction in global colonic score in those patients who reported subjective improvement, but this was not accompanied by any change in the objective assessment of bowel habit [Table 12]. The reduction in global score reflected a reduction in pain score but the pain score change was not of sufficient magnitude to account for the whole global score change - the difference seems to reflect changes in other elements within the global scoring system.

This may reflect genuine changes in these parameters. An alternative explanation is that the score accorded to these factors is modulated to a

greater degree by other factors in the complex process by which patients perceive, evaluate, and attribute symptoms.

The pain score is a relatively crude method of analysing the pain of IBS which varies in intensity, site and character. Further, it has been known for decades that perception and reporting of pain is much influenced by psychological variables (Livingston 1953), and pain is a common symptom in psychiatric outpatients (Mersky and Spear 1967).

Table 11. *Comparison of Improved and Not Improved Groups. (mean scores)*

	Improved	Not Improved	Diff	SED	t
	n=27	n=15			
Symptom duration (years)	3.9	3.8	0.1	1.4	0.03
Fibre intake (g / day)	19.1	23.1	4.1	2.1	1.9
range	12 - 29	7 - 31			
Initial pain score	6.0	7.1	1.1	1.7	0.7
range	0 - 16	7 - 31			
Initial frequency score	10.2	13.0	2.8	2.4	1.2
range	4 - 30	2 - 28			
Initial constipation score	31.3	43.0	12.7	10.2	1.2
range	6 - 130	3 - 141			
Initial global score	7.4	7.1	0.3	0.7	0.5
range	2 - 11	4 - 12			

not significant

Table 12. *Association between the reduction in symptom scores and assessment of general well-being. (mean scores)*

		Improved	Not Improved	Diff	SED	t
		n=27	n=15			
Pain		2.6	0.5	2.1	1.4	1.5
	range	-1 - 10	-3 - -5			
Frequency		1.0	0.3	0.7	1.6	0.4
	range	-2 - 9	-4 - 11			
Constipation		4.0	-2.4	6.4	6.3	1.0
	range	-10 - 52	-8 - 32			
Global		4.6	1.6	3.0	0.8	4.0 **
	range	0 - 8	-2 - 7			

** $p < 0.01$

Effect of treatment

The treatment groups did not differ in any of the examined parameters which were considered likely influences on outcome [Table 13]. After three months the outcome in both groups, was independant of treatment group [Table 14]. There was no difference in the proportion of subjects who reported feeling 'generally better' ; 59 per cent (fibre supplemented) vs 70 per cent (placebo) [Table 15]. Nor was there any significant difference in the initial changes in specific IBS symptoms between the groups [Tables 16 - 19]. The inter-relationship between the reduction in symptom scores, treatment, initial symptom scores, and psychometric assessment is examined in Tables 20 - 23.

Although some studies have shown symptomatic improvement with fibre supplementation (Manning 1977, Prior et al 1987, Kumar et al 1987), a greater number have reported no significant advantage over placebo (Hillman et al 1984, Soltoft et al 1976, Longstreth et al 1981, Arthurs 1983, Lucey 1987, Arffmann et al 1986). A consensus has developed that dietary fibre supplementation can reduce constipation but that it has little more than a placebo effect on the other symptoms which characterise IBS.

Our patients all had a long history of abdominal symptoms and none had previously taken bran supplements for a sustained period as treatment for their symptoms. This is a considerable exclusion, given that dietary 'fibre' is the treatment of first resort for most physicians when faced with a patient with a putative diagnosis of IBS/idiopathic constipation. The patients had similar daily fibre intake to that of the general population. Fibre intake was increased by approximately 20 per cent to around 25g / day in the treated group. This relatively small increment may account for the low incidence of reported side effects and low drop out rate. On the other hand, those patients who did not improve might have done so with a greater fibre supplementation than was practicable using this concentrated tablet formulation.

Table 13. *Treatment groups : Initial characteristics. (mean [SD])*

Treatment Group	A	B
	n = 25	n = 24
sex ratio (male:female)	9 : 16	8 : 16
age (years)	39.2 [13.0]	39.8 [13.0]
range	18 - 76	20 - 65
daily fibre intake (g)	20.9 [6.6]	19.4 [4.9]
range	7 - 31	10 - 30
symptom duration (years)	3.4 [3.3]	4.2 [4.9]
range	0.25 - 10	0.25 - 11
initial pain score	5.9 [5.1]	6.8 [5.1]
range	0 - 18	0 - 17
initial frequency score	10.4 [6.5]	11.1 [8.2]
range	2 - 30	3 - 28
initial constipation score	31.0 [23.1]	36.3 [38.7]
range	3 - 141	4 - 108
initial global score	7.4 [2.3]	7.1 [2.6]
range	2 - 12	2 - 11
		not significant

Table 14. *Effect of Treatment on Outcome ; objective measures of outcome (reduction in symptom scores between week 0 and week 12)*

Treatment group	A	B	Diff	SED	t
	n = 22	n = 20			
Mean reduction in					
Pain score	1.4	2.4	-1.0	1.2	0.8
range	-2 - 6	-3 - 10			
Frequency score	-0.1	1.5	-1.6	1.4	1.2
range	-2 - 11	-4 - 9			
Constipation score	-3.1	6.8	-9.9	5.3	1.9
range	-10 - 32	-8 - 52			
Global score	3.0	3.8	-0.8	0.8	1.0
range	-2 - 8	-1 - 7			

not significant

Table 15. *Effect of Treatment on Outcome ; subjective self-evaluation of change between week 0 and week 12.*

Treatment group	A	B
	n = 25	n = 24
Improved	13	14
Not improved	9	6

not significant

Table 16. Comparison of Improved and Not Improved Groups in treatment group A ; initial characteristics. Mean scores

	Improved	Not Improved	Diff	SED	t
	n = 13	n = 9			
Symptom duration (years)	3.2	4.3	1.1	1.5	0.8
range	0.25 - 7	0.25 - 10			
Fibre intake (g/day)	19.4	23.1	3.7	3.0	1.2
range	7 - 27	11 - 31			
Initial pain score	4.5	8.0	3.5	2.2	1.2
range	0 - 12	2 - 18			
Initial frequency score	8.8	13.2	4.4	2.8	1.6
range	2 - 70	5 - 62			
Initial constipation score	24.2	42.1	17.0	9.7	1.9
range	3 - 119	12 - 141			
Initial global score	7.2	6.7	0.5	1.1	0.5
range	3 - 12	2 - 11			

not significant

Table 17. *Comparison of Improved and Not Improved Groups in treatment group A ; reduction in symptom scores. (mean)*

		Improved	Not Improved	Diff	SED	t
		n = 13	n = 9			
pain score		1.5	1.0	0.5	1.8	0.3
	range	-1 - 6	-2 - 5			
frequency score		-1.0	1.2	-2.2	1.8	1.2
	range	-2 - 8	-1 - 11			
constipation score		-4.2	-1.2	-2.3	5.1	0.5
	range	-10 - 20	-8 - 32			
global score		4.5	0.9	3.6	0.9	3.9 ***
	range	0 - 8	-2 - 6			

*** $p < 0.001$

Table 18. *Comparison of Improved and Not Improved Groups in treatment group B ; initial characteristics. (mean)*

	Improved	Not Improved	Diff	SED	t
	n = 14	n = 6			
Symptom duration (years)	4.5	3.0	1.5	2.5	0.6
range	0.25 - 12	1 - 6			
Fibre intake (g/day)	18.6	23.0	4.4	3.2	1.4
range	10 - 26	12 - 30			
Initial pain score	7.5	5.6	1.9	2.6	0.7
range	2 - 26	0 - 15			
Initial frequency score	11.5	12.6	1.1	4.2	1.3
range	4 - 21	3 - 28			
Initial constipation score	36.5	44.6	8.1	20.1	0.4
range	4 - 108	8 - 82			
Initial global score	7.6	7.8	0.2	0.8	0.2
range	2 - 9	4 - 11			

not significant

Table 19. *Comparison of Improved and Not Improved Groups in treatment group B ; reduction in symptom scores. (mean)*

		Improved n = 14	Not Improved n = 6	Diff	SED	t
pain score		3.7	-0.4	4.1	2.2	1.9
	range	0 - 10	-3 - 4			
frequency score		0.8	-1.4	4.2	2.8	1.5
	range	-2 - 9	-4 - 4			
constipation score		11.6	-3.4	15.0	12.1	1.2
	range	4 - 52	-8 - 22			
global score		4.6	2.8	1.8	1.3	1.5
	range	0 - 6	-1 - 7			

not significant

Table 20. *Association between the reduction in pain score and initial parameters [According to treatment groups].*

	r		R	
Treatment group	A	B	A	B
	n = 22	n = 20	n = 22	n = 20
Symptom duration	-0.31	-0.36 *	-0.30	-0.33
Fibre intake	-0.24	-0.18	-0.15	0.02
Initial pain score	0.23	0.66 **	0.16	0.41
Initial frequency score	-0.40	0.08	-0.47 *	0.21
Initial constipation score	-0.49 *	0.04	-0.68 **	0.22
Initial global score	0.18	0.23	0.12	0.07
Anxiety				
VAS	-0.42	-0.54 *	-0.30	0.16
Questionnaire	-0.37	-0.49	-0.03	-0.31
Depression				
VAS	-0.35	-0.62 *	-0.27	0.45
Questionnaire	-0.40	-0.57 *	-0.30	-0.19

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

** $p < 0.01$
* $p < 0.05$

Table 21. *Association between the reduction in frequency score and initial parameters [According to treatment groups].*

	r		R	
Treatment group	A	B	A	B
	n = 22	n = 20	n = 22	n = 20
Symptom duration	0.00	0.19	-0.07	0.21
Fibre intake	-0.21	0.11	-0.03	0.19
Initial pain score	0.31	-0.17	-0.03	-0.10
Initial frequency score	0.68 **	0.68 **	0.66 **	0.55 *
Initial constipation score	0.39	0.61 **	0.45	0.54 *
Initial global score	-0.27	-0.25	-0.39	-0.28
Anxiety				
VAS	-0.10	0.35	-0.10	0.12
Questionnaire	-0.16	0.29	0.09	0.13
Depression				
VAS	0.03	-0.05	-0.02	0.11
Questionnaire	0.15	0.01	-0.19	0.22

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

** $p < 0.01$
* $p < 0.05$

Table 22. *Association between the reduction in constipation score initial parameters [According to treatment groups].*

	r		R	
Treatment Group	A	B	A	B
	n = 22	n = 20	n = 22	n = 20
Symptom duration	-0.19	0.35	-0.28	0.48
Fibre intake	0.02	0.16	-0.04	0.24
Initial pain score	-0.27	-0.17	-0.49 *	-0.04
Initial frequency score	0.26	0.77 ***	0.07	0.82 ***
Initial constipation score	0.49 *	0.74 ***	0.38	0.81 ***
Initial global score	-0.35	-0.27	-0.34	-0.37
Anxiety				
VAS	-0.19	0.15	0.11	0.20
Questionnaire	0.08	0.21	-0.12	0.31
Depression				
VAS	0.22	-0.28	0.15	-0.10
Questionnaire	0.19	0.07	0.22	0.03

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

*** $p < 0.001$
* $p < 0.05$

Table 23. *Association between the reduction in global score and initial parameters [According to treatment groups].*

	r		R	
Treatment group	A	B	A	B
	n = 22	n = 20	n = 22	n = 20
Symptom duration	-0.14	0.17	-0.24	0.09
Fibre intake	-0.56 *	0.39	-0.53 *	0.42
Initial pain score	-0.13	-0.03	-0.11	-0.11
Initial frequency score	-0.32	0.32	-0.27	0.54 *
Initial constipation score	-0.29	0.25	-0.40	0.40
Initial global score	0.29	0.13	0.22	0.18
Anxiety				
VAS	-0.49 *	0.01	-0.43	0.16
Questionnaire	-0.31	-0.12	-0.27	0.19
Depression				
VAS	-0.16	-0.14	-0.15	-0.06
Questionnaire	-0.21	0.09	0.06	-0.12

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

* $p < 0.05$

Outcome and psychometric score

Those subjects who felt 'generally better' after treatment had scored significantly lower in the initial assessments of depression than the other subjects. There was a trend towards lower scores in the assessments of anxiety in those who felt 'generally better' but this did not reach conventional levels of significance [Table 24].

The treatment groups were very similar in terms of psychometric scores [Table 25].

Initial depression ratings were a better predictor of improvement during the study period than any of the other parameters including inclusion in the fibre supplemented group.

Table 24. *Outcome and Psychometric Score. (mean)*

	Improved	Not improved	Diff	SED	t
	n = 22	n = 20			
Anxiety					
VAS	34.9	43.3	8.4	4.7	1.78
range	11 - 89	16 - 89			
Questionnaire	1.4	2.5	1.1	0.5	1.99
range	0 - 9	0 - 9			
Depression					
VAS	26.2	35.6	9.4	3.9	2.43 *
range	14 - 70	4 - 67			
Questionnaire	0.7	2.6	1.9	3.8	2.86 **
range	0 - 5	0 - 4			

** $p < 0.01$
* $p < 0.05$

Table 25. *Initial psychometric scores according to treatment group. (mean [SD])*

Treatment Group	A	B
Anxiety		
VAS	41.6 [18.1]	36.3 [15.0]
range	14 - 67	11 - 89
Questionnaire	1.9 [1.8]	1.7 [1.5]
range	0 - 5	0 - 7
Depression		
VAS	30.6 [16.4]	31.0 [11.7]
range	11 - 49	4 - 70
Questionnaire	1.2 [1.9]	0.9 [1.6]
range	0 - 3	0 - 5

not significant

Table 26. *Comparison of Improved and Not Improved Groups in treatment group A ; initial psychometric scores. (mean)*

	Improved	Not Improved	Diff	SED	t
	n = 13	n = 9			
Anxiety					
VAS	34.5	48.9	14.4	7.5	1.9
range	14 - 67	25 - 89			
Questionnaire	1.7	2.4	0.7	0.8	1.1
range	0 - 4	0 - 5			
Depression					
VAS	24.7	39.7	15.0	6.0	2.2 *
range	14 - 49	11 - 47			
Questionnaire	1.1	1.4	0.3	0.6	2.0
range	0 - 3	0 - 3			

* $p < 0.05$

Table 27. *Comparison of Improved and Not Improved Groups in treatment group B ; initial psychometric scores. (mean)*

	Improved	Not Improved	Diff	SED	t
	n = 14	n = 6			
Anxiety					
VAS	39.4	33.5	5.9	7.9	0.7
range	11 - 89	16 - 70			
Questionnaire	1.8	2.0	0.2	0.2	1.0
range	1 - 6	0 - 9			
Depression					
VAS	30.8	28.3	2.5	6.0	0.4
range	16 - 70	4 - 67			
Questionnaire	1.0	0.7	0.3	0.3	0.9
range	0 - 5	0 - 4			

not significant

FIVE YEAR FOLLOW-UP STUDY

Recruitment

The study population was a cohort of 75 consecutive patients referred to a gastrointestinal outpatient clinic, diagnosed as suffering from irritable bowel syndrome and recruited over a three month period, five years previously.

Diagnosis

The diagnosis was made on the basis of an altered bowel habit (unaccompanied by rectal bleeding) of at least three months duration, abdominal pain present most days and frequently relieved by defaecation, and abdominal distension, without symptoms of systemic upset.

Assessment : gastrointestinal symptoms

At the initial assessment all patients completed a 34 item questionaire examining gastrointestinal symptoms. This was self administered and requested details of symptoms in the previous three months. At initial assessment answers to every question was obtained by, if necessary, further explanation to the patient. In the postal survey this was clearly not possible.

Five years after the initial assessment patients were sent a postal questionnaire (using many of the same questions as the original questionnaire) which sought information on present symptoms and treatment, and on events since the diagnosis [Appendix 4]. A single telephone request for cooperation was made four weeks after postal contact if no reply had been received.

From the questionnaires symptom scores were calculated for;

stool frequency	(number of stools / week)
straining at stool	(range 0-4)
hard or pellety stool	(range 0-4)
urgency to defaecation	(range 0-4)
abdominal pain	(range 0-4)
relief of pain with defaecation	(range 0-2)
sensation of incomplete emptying	(range 0-4)

Reported estimates of such bowel and gastrointestinal functions show reasonable correlation with detailed calendar diaries of bowel habit (Manning et al 1976).

Assessment : general well-being

An overall assessment of well-being was also sought;

'How is your tummy trouble now compared to when you first attended this hospital ?'

Possible responses were 'unchanged', 'better' or 'worse'.

Use of medications

Details were sought regarding the use of prescribed medications, of self medication (including laxatives), and of 'alternative therapies'.

Psychological assessment

A modified Middlesex Hospital Questionnaire was used to assess psychological status. The questionnaire included the same items assessing depression and anxiety as had been used 5 years previously. The Crown Crisp Experiential Index (CCEI) is an objective and valid technique which gives information similar to that obtained by formal psychiatric assessment at interview, at least in terms of the likely psychiatric 'caseness' or diagnoses (Crown and Crisp 1979). In the initial study the full 48 item questionnaire was used. It was thought unlikely that subjects would respond to a postal questionnaire if it was 20-30 pages long : therefore the number of individual questions was minimised.

In the previous study only those questions examining phobic anxiety, free floating anxiety, and depression were considered useful in differentiating between those with functional disorders and those with organic diagnoses. The follow-up questionnaire was restricted to the eight questions in each of these subsets :

'FFA'. Anxiety without identifiable cause.

'PHO' Anxiety which is limited to particular situations and which does not occur outwith those situations.

'DEP' Sadness of mood accompanied by psychomotor blunting or slowing.

Each item scores 0-2 and each subset therefore a total of 0-16 [Appendix 5]. Only the FFA and DEP subsets are reported here.

Psychological assessment

Depression and anxiety were also assessed by a visual analogue scale. This method has been validated on a horiziontal linear model (Ingham 1965, Ingham and Miller 1976).

Of the 75 patients studied originally, three had died of unrelated disease, and the whereabouts of 13 could not be traced. Of the remainder, 43 patients (73%), returned completed questionnaires. 16 patients failed to respond to a second postal invitation and/or a telephone request.

The characteristics of the respondents are shown in Table 28. Those patients who did not reply to the five year follow-up questionnaire were not significantly different from the respondents in the following parameters at initial assessment ; age, duration of symptoms, severity of initial symptoms, or initial anxiety and depression ratings.

Outcome

28 patients (65%) reported that their 'tummy trouble was better than when first seen at the clinic', 13 (30%) reported 'unchanged', and 2 (5%) 'worse'. The only gastrointestinal symptom which showed a significant correlation with overall assessment was pain; those patients who felt their 'tummy trouble was better' had significantly lower pain scores five years after initial referral. There was no similar correlation between the overall assessment and other gastrointestinal symptoms (initial or five year absolute levels or the change over the period) [Tables 29 & 30].

Table 28. *Subject characteristics. (mean (SD))*

	total	'better'	'unchanged/worse'
	n=43	n=28	n=15
sex ratio (f : m)	27 : 16	18 : 10	9 : 7
enhanced dietary fibre at five years	27 [63%]	20 [74%]	7 [46%]
symptom duration (months)	50.1 (61)	42.1 (59)	66.0 (62)
range	3 - 240	3 - 240	6 - 240
age (years)	39.2 (10.9)	39.7 (11.2)	38.3 (10.5)
range	18 - 60	18 - 60	24 - 59
			not significant

Table 29. *Relationship between outcome and initial gastrointestinal symptom scores. (mean (SD))*

	'better' n=28	'unchanged/worse' n=15
stool frequency	11.5 (7.8)	12.1 (10.1)
range	2 - 35	1 - 30
straining at stool	1.7 (1.5)	1.5 (1.1)
range	0 - 4	0 - 4
hard or pellety stool	1.6 (1.6)	1.4 (1.2)
range	0 - 4	0 - 4
urgency to defaecation	1.8 (1.4)	1.5 (1.6)
range	0 - 4	0 - 4
abdominal pain	2.5 (1.4)	2.3 (1.2)
range	0 - 4	0 - 4
relief of pain at defaecation	1.3 (0.8)	1.1 (0.8)
range	0 - 2	0 - 2
sensation incomplete emptying	2.0 (1.4)	1.6 (1.1)
range	0 - 4	0 - 4

not significant

Table 30. *Relationship between outcome and gastrointestinal symptom scores after 5 years. (mean (SD))*

	'better' n=28	'unchanged/worse' n=15
stool frequency [per week]	9.6 (6.7)	11.5 (7.7)
straining at stool	1.1 (1.0)	1.4 (1.2)
range	0 - 4	0 - 4
hard or pellety stool	1.1 (1.3)	1.5 (1.9)
range	0 - 4	0 - 4
urgency to defaecation	1.5 (1.2)	1.4 (1.4)
range	0 - 4	0 - 4
abdominal pain	1.3 (1.1)	2.3 (1.6) **
range	0 - 4	0 - 4
abdominal pain : change	-1.2 (1.7)	-0.1 (1.5) **
range	-4 - +1	-2 - +2
relief of pain at defaecation	1.4 (0.8)	1.1 (0.7)
range	0 - 2	0 - 2
sensation incomplete emptying	1.6 (1.3)	2.1 (1.3)
range	0 - 4	0 - 4

** $p < 0.01$

The relationship between anxiety scores and five-year general outcome is shown in Table 31. The trend was clearly for those patients who reported feeling 'better' to record lower scores at initial assessment and at the five year reassessment than those who reported feeling 'unchanged' or 'worse'. However, the difference between the outcome groups did not achieve statistical significance at the conventional $p < 0.05$ level.

In both groups there was a trend to reduced anxiety scores after the five year interval but in neither group was this change significant, and the magnitude was similar in the groups [Table 31].

There was no difference in initial or five year depression scores between those patients who were 'better' and those who were not [Table 31].

Table 31. *Relationship between outcome and scores for anxiety and depression. (mean)*

		'better' n=28	'unchanged/worse' n=15	p
initial anxiety		6.3	8.7	0.06
	range	0 - 14	3 - 14	
five year anxiety		5.3	7.9	0.05
	range	0 - 12	0 - 13	
initial depression		4.6	5.5	0.62
	range	0 - 10	2 - 12	
five year depression		3.3	3.7	0.55
	range	0 - 10	2 - 7	

(Mann Whitney U test)

Medications

53% of patients were taking no regular medications. No patients were taking medications for other complaints. In the 22 patients (47 per cent) taking prescribed treatment (other than laxatives) each week for gastrointestinal symptoms, mebeverine was the drug used most often. Seven patients were taking more than one medication on a regular basis. Five patients (12 per cent) were taking 'bulking' laxatives regularly. No other laxatives were being used. A single patient reported taking a tranquilliser. There was no difference between the outcome groups in the use of medications.

Three patients had had treatment for 'nerves'. 77 per cent of patients thought that 'worry or nerves usually upset their tummy trouble'. One patient had found meditation of help. Only one other 'alternative' approach had been tried one patient reported no effect of herbalism (other treatments had likewise failed to effect an improvement).

Dietary Fibre

63 per cent of patients had increased their dietary fibre intake in an effort to reduce their symptoms, and were persisting with that change. No patients reported that they avoided specific foodstuffs, but one reported that alcohol exacerbated her symptoms. Two patients had been referred in the intervening years to another clinic with the same symptoms ; in both cases the diagnosis (as reported by the patient) was unchanged.

Clinic visit

Eight patients (19 per cent) thought that the gastrointestinal clinic visit and the treatment and advice they had received had been of no help, six (14 per cent) judged it completely helpful, and 29 (67 per cent) partially helpful. These groups did not differ in respect of age, initial gastrointestinal symptoms, or in the initial or five year anxiety and depression ratings. The duration of symptoms in these groups were 30.3 months, 65.3 months and 11.3 months respectively.

This study confirms the persistence of troublesome GI symptomatology in a substantial minority (here 35 per cent) of IBS patients. No alternative diagnosis had emerged during the five year follow-up, attesting the accuracy of the initial diagnosis. The majority of respondents continued to adhere to a high fibre diet. At the time of the initial visit our standard approach to patients with patients with IBS was to recommend a high fibre diet after a detailed explanation of the condition, emphasising the benign long-term course and the influence of psychological factors.

BIOCHEMICAL PARAMETERS

A biochemical parameter which afforded an objective measure of the emotional response to 'stress', or which reflected the degree of anxiety or depression engendered, would clearly be of great value. Previous attempts to find such a parameter have been disappointing, making little impact on routine assessment. Review of the literature revealed several possible candidates but many had drawbacks which would have made their use in routine clinical practice impossible, at least in the foreseeable future. I was concerned to investigate parameters which might prove a practical, reliable guide to psychological components of the IBS symptom complex.

Bartrop et al (1977) were first to demonstrate that emotional state might influence aspects of immunocompetence. In bereaved subjects there was reduced lymphocyte response to mitogens, although there was no difference in lymphocyte numbers, immunoglobulin concentrations, autoantibody profiles, or plasma cortisol levels. Severe depression can diminish components of the immune response (Schleifer et al 1985 , Kronfol et al 1983).

Academic stress is reported to cause several changes in immunocompetence;

1. Mitogen responsiveness of lymphocytes is reduced (Dorian et al 1982).
2. T helper-cell proportion is increased (Baker et al 1985).
3. Salivary secretory immunoglobulin A (sIgA) production is enhanced. Jemmott et al (1983) reported that the rate of salivary IgA production might be reduced by academic stress, a phenomenon which was modulated by personality factors.

Salivary IgA concentration is probably inversely related to flow rate, and the rate of saliva production is clearly influenced by mood ; witness the dry mouth of extreme fright or acute anxiety. Stone et al (1987) have argued that mood-related modulation of salivary IgA production is therefore a poor measure of immune function.

However it was not the purpose of this study to advance this arguement ; rather I sought to establish whether salivary IgA might be a clinically useful measure of mood or response to stress in IBS patients.

Saliva collection and analysis

Saliva samples were collected as follows :

Specimens were collected between one and four pm from seated, rested, subjects who were alone in the examination room. Subjects had not eaten or drunk anything, smoked, or cleaned their teeth, in the hour before collection, and were asked not to cough prior to spitting.

Subjects with infection or ulceration of the mouth, or with active dental caries or gum disease (of greater than clinically mild severity) were excluded.

Subjects spat unstimulated saliva into a universal container for 5 minutes. The whole saliva was quantified using a 20ml syringe which was also used to transfer it into a 10 ml stoppered plastic or glass tube such as is used for clotted blood specimens.

The specimen was immediately frozen and stored at 4°C.

Salivary IgA was subsequently assessed by immunoturbidimetry on a Monarch centrifugal fast analyser (adapted from Wenham and Horn 1980).

Blood collection and analysis

Immediately after collection of the saliva a 20 ml sample of venous blood was drawn from the relaxed subjects' antecubital fossa, using a tourniquet. Serum IgA levels were likewise assayed by immunoturbidimetry (Wenham and Horn 1980).

There was no correlation between salivary IgA concentration or its' rate of production and the salivary amylase or Na concentration [Table 34]. Salivary IgA and its' rate of production was similar in IBS patients to that found in the general population. As in previous reports there was no correlation between serum and salivary IgA (Finkelstein et al 1984) [Table 33]. There was no correlation with the measures of stress (anxiety and depression) used in this study [Table 36 & 38]. It therefore seems unlikely that salivary IgA will be useful in identifying those IBS sufferers in whom such anxiety and/or depression are predominant determinants of the sickness behaviour. Further studies may permit correlation between the rate of salivary IgA production and initial symptom assessments.

I have no ready explanation for the relationship between salivary IgA concentration and bowel habit [Table 37]. The salivary IgA concentration is increased as the bowel habit is less constipated (frequency and constipation scores increase). This may indicate an undefined correlation between bowel habit and salivary IgA but may equally represent a chance finding - there is no correlation with the rate of IgA production [Table 35].

Table 32. *Serum and Salivary IgA. (n = 49)*

	mean	range	SD
Salivary IgA IU / ml	7.25	2.0 - 21.2	2.3
Salivary IgA IU / min	3.4	0.5 - 10.7	2.1
Serum IgA iu / ml	126	44 - 246	52

Table 33. *Association between serum and salivary IgA. (n = 49)*

	r	R
salivary IgA concentration	-0.12	-0.15
salivary IgA production rate	0.01	0.00

Table 34. *Association between IgA and other salivary constituents. (n = 49)*

	r	R
salivary Na	0.13	0.10
salivary amylase	0.33	0.23

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

not significant

Table 35. *Relation between Salivary IgA production rate [IU / min] and symptoms. (n = 49)*

	r	R
initial pain score	0.13	0.08
initial frequency score	0.23	0.19
initial constipation score	0.21	0.28
initial global score	0.16	0.17
change in pain score	-0.12	-0.16
change in frequency score	0.01	0.13
change in constipation score	0.24	0.35
change in global score	-0.07	-0.10

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

not significant

Table 36. *Relation between Salivary IgA production rate [IU / min] and psychometric assessment. (n = 49)*

	r	R
Anxiety		
VAS	-0.08	-0.11
Questionnaire	0.17	0.12
Depression		
VAS	0.01	0.09
Questionnaire	-0.09	0.01

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

not significant

Table 37. *Relation between Salivary IgA concentration [IU / ml] and symptoms. (n = 49)*

	r	R
initial pain score	-0.18	-0.15
initial frequency score	0.37 *	0.21
initial constipation score	0.43 **	0.37 *
initial global score	-0.23	-0.31
change in pain score	-0.05	0.01
change in frequency score	0.59 ***	0.40 *
change in constipation score	0.73 ***	0.38 *
change in global score	-0.01	-0.08

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

*** $p < 0.001$
** $p < 0.01$
* $p < 0.05$

Table 38. *Relation between Salivary IgA concentration [IU / ml] and psychometric assessment. (n = 49)*)

	r	R
Anxiety		
VAS	0.08	-0.02
Questionnaire	-0.10	-0.03
Depression		
VAS	0.10	0.16
Questionnaire	-0.15	-0.18

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

not significant

Table 39. *Relationship between Salivary IgA and general outcome. (mean)*

	Improved	Not improved	Diff	SED	t
	n = 22	n = 20			
Salivary IgA (IU / ml)	77.7	69.2	8.5	10.4	0.8
range	31 - 212	10 - 84			
Salivary IgA (IU / min)	41.0	35.6	5.4	8.0	0.7
range	20 - 94	8 - 107			

not significant

The sympathetic nervous system is one pathway via which psychological influences on physiological function might be mediated. It is now generally accepted that urinary adrenaline is elevated by various mental stresses, and seems to correlate with subjective feelings of distress (Frankhauser 1975, Baum et al 1985). Noradrenaline is more sensitive to posture and exercise. Among the most potent stressors are anticipation of threat and emotional challenge (Johanssen et al 1983).

Since plasma catecholamines are unaffected by excretory processes and renal function, they are thought by some to reflect sympathetic output more accurately than urinary catecholamines. However there are several important confounding factors ;

1. the influence of drugs, exercise, beverages, posture, circadian rhythm, menstrual cycle, and age (Christensen 1983).
2. the collection and storage of samples can introduce significant errors (Carruthers et al 1970)
3. the half lives of adrenaline and noradrenaline are 12 minutes only and hence reflect very short term responses.
4. assays on antecubital blood estimates predominantly forearm-tissue - derived catecholamine. This is much influenced by exercise and as the plasma adrenaline concentration increases with stress, so too does adrenaline extraction across the forearm (Jorgensen et al 1985).

For these reasons it was considered extremely unlikely that plasma catecholamines could possibly represent a rapid, practical, routine assessment of the level of anxiety / depression.

Methodological difficulties also dog the routine use of urinary catecholamines in clinical practice (Ward and Mefford 1985) :

1. consumption of coffee and alcohol, smoking, and medication may influence catecholamine levels in blood and urine.
2. with stress the compartmentalisation of catecholamines may change, influencing urinary concentrations obtained.
3. changes in catecholamines can be very rapid and may reflect short term emotional states.
4. renal function can interfere with urinary catecholamines.

   Although it seems that urinary excretion mirrors the circulating levels of adrenaline and noradrenaline the influence of renal function has not been fully assessed. The renal nerves are a potential confounding source of noradrenaline (in dogs urinary noradrenaline is arterial plasma-derived (Kopp et al 1983).

I did however study urinary catecholamine in the first 15 patients in the therapeutic trial and examined the relationship between this parameter, salivary IgA, the assessments of anxiety and depression and outcome in the therapeutic trial.

Methodology

24 hour volumes of urine were collected from 15 patients who were subjects of the fibre supplementation study, before the treatment was commenced. The importance of complete collection was emphasised. Patients were excluded if they complained of specific urinary or genitourinary symptoms or if there was any history of flushing, hypertension, kidney stones or renal impairment.

Urinary free metanephrine was assayed by radioimmunoassay.

Results and Analysis

There is a poor correlation between 24-hour urinary metanephrines and VAS and questionnaire assessments of anxiety and depression. [Table 43] Perhaps the assessment would have been better performed before enrollment into the trial. The process of enrollment included some explanation of IBS, in order that informed consent be obtained, and this may have ameliorated some of the arousal associated with anxiety. In any event catecholamines may reflect shorter term emotional states of arousal and/or worry than those which are concerned in the development and maintenance of IBS.

The patients were representative of those from the clinical trial cohort as a whole.

Table 40. *Subjects : Initial characteristics. (n = 10)*

	mean	range
age (years)	36	20 - 64
sex ratio (male:female)	9 : 6	
daily fibre intake (g)	18.9	12 - 28
symptom duration (months)	28.2	3 - 72
pain score	5.6	4 - 14
frequency score	12.2	3 - 24
constipation score	28.6	7 - 112
global symptom score	6.9	2 - 11

Table 41. *Urinary free metanephrine (ug / 24 hours).*

	n	mean	range	SD
overall	15	2.26	1.34 - 3.3	0.86
improved	9	2.17	1.34 - 2.9	0.72
not improved	6	2.93	1.45 - 3.3	0.78

not significant

Table 42. *Correlation between urinary metanephrine and gastrointestinal symptoms. (n = 15)*

	r	R
initial pain score	0.25	0.32
initial frequency score	0.05	-0.18
initial constipation score	0.12	0.19
initial global score	0.35	0.39
change in pain score	0.40	0.47
change in frequency score	0.03	-0.20
change in constipation score	0.09	0.16
change in global score	0.40	0.38

r = product-moment correlation coefficient not significant
R = Spearman coefficient of rank correlation

Table 43. *Correlation between urinary metanephrine and psychometric scores. (n = 15)*

	r	R
anxiety		
VAS	-0.27	-0.39
Questionnaire	0.35	0.31
depression		
VAS	0.29	0.20
Questionnaire	0.40	0.39

r = product-moment correlation coefficient not significant
R = Spearman coefficient of rank correlation

The physiological role of serotonin has been the subject of much scrutiny and speculation. That serum contained a vasoactive substance was known for many decades before Rapport et al (1948) isolated the substance, and identified it as 5-hydroxytryptamine [3-(-aminoethyl)-5-hydroxyindole] (serotonin). Most of the bodies' serotonin is found in the enterochromaffin cells of the gastrointestinal tract (Erspamer 1954). It is synthesised by hydroxylation and decarboxylation of tryptophan in situ, as is the serotonin in most tissues. Within the enterochromaffin cells serotonin has a half life of approximately 15 hours. Release of serotonin into the intestinal circulation and into the gut lumen is increased by several factors ; mechanical stimulation, hypertonicity, feeding (Ferrara et al 1984), acidity, norepinephrine, and vagal influences (Ahlman et al 1981). The serotonin released into the enteric circulation is rapidly cleared from the plasma by uptake and degradation by endothelial cells, notably in the liver and lungs and by platelet uptake. However it seems that a relatively small proportion of gut 5-HT is taken up by platelets (Anderson et al 1985). The physiological significance of serotonin in the gastrointestinal tract is still not fully understood.

Circulating serotonin is almost all contained in the platelets, though perhaps 20 per cent is bound to plasma protein (Demet et al 1978). Within the

platelets serotonin is stored in one of the three platelet granule types, the osmophillic dense granules ; the mechanism by which it is pumped into the granule is similar to that for catecholamines. Most, if not all, of this platelet-granule-bound serotonin is thought to originate in the enterochromaffin cells, platelets themselves being unable to synthesise serotonin.

Platelets take up serotonin during passage through the enteric vessels by way of a high affinity, active uptake mechanism. This system is similar to that found in trytaminergic nerve endings which allows re-uptake of released transmitter. The turnover of serotonin in platelets is relatively slow with a half life of several days (Heysell 1961).

The physiological effects of serotonin are often variable. This variability reflects the reflex, and therefore conditional, nature of many of the effects, and tachyphylaxis, which is common in serotonin mediated changes. The wide range of susceptibility to blocking agents points to the existence of several different serotonin receptors. Among the physiological effects of serotonin which have been demonstrated are ;

1. The induction of platelet aggregation (Laubscher and Pletscher 1979). The function of platelet serotonin remains unestablished.
2. Vasoactive properties. Serotonin can cause both constriction and dilatation depending on the vascular bed involved, its

resting tone, and the concentration of serotonin. Similarly cardiac output may be increased or decreased.

3. Gastrointestinal motility regulation. Small intestinal motility is stimulated by infusion of serotonin, while motility in the stomach and colon is reduced (Misiewicz et al 1966). Enterochromaffin cells also contain substance P and motilin, two other potent motility regulators. In carcinoid syndrome, with its characteristic diarrhoea, the small intestine is known to be hypermotile and the colon relatively quiescent. Further, cholera toxin is a potent serotonin releasing agent (Cassuto et al 1980). But in rats enteric motility is not effected by virtually denuding the intestine of serotonin by feeding a tryptophan free diet. Non-mucosal enteric 5-HT, found in the enteric neurones (Feldberg and Toh 1953), is considered by some to be a local neurotransmitter (Gershon and Erde 1981). The role of serotonin in the normal control of motility is unestablished.

4. Neurotransmission. Much of the interest in serotonin centred on its role in central nervous system (cns) transmission processes. Within the cns the cell bodies of serotoninergic neurones are found almost exclusively in the raphe nucleus of the brain stem. Cns serotonin is synthesised in situ. Circulating serotonin is thought to have few central effects as it penetrates the blood-brain barrier very poorly. However tryptophan

injections can cause increases in brain serotonin levels within an hour in animal models (Ternaux et al 1981). The concentration of cns serotonin may thus be regulated by diet through changes in tryptophan. Precursor availablility seems to limit the rate of neurotransmitter synthesis. Serotoninergic mechanisms have been implicated in pain perception, in sleep regulation, and in control of behaviour and arousal (particularly in affective disorders). Central control of temperature and blood pressure control are also influenced by serotonin. However the precise mechanisms by which serotonin influences such systems have not yet been elucidated. The handling of serotonin in platelets is similar to that in serotoninergic neurones (Todrick and Tait 1969). Platelets have been proposed as a model for the study of serotonin behaviour in and around such neurones (Pletscher 1978).

Changes in platelet serotonin have been reported in depression (Le Quan Bui et al 1984), migraine (Hilton and Cummimgs 1980, Hannington 1978), carcinoid syndrome (Grahame-Smith 1977), cirrhosis, premenstrual tension, and hypertension (Bargava et al 1979, Mehta and Mehta 1981).

Estimation of serotonin.

The estimation of serotonin in platelets avoids many of the pitfalls of measuring whole blood hydroxyindoles. Here difficulties in serotonin extraction can lead to erroneous results and HIAA may also be included in the estimation (Stacey 1966).

Platelet serotonin was assayed by high pressure liquid chromatography (Tagari et al 1984). [Appendix 6]

Subjects

In a pilot study, 16 subjects were drawn from the clinics and wards of the Gastrointestinal Unit. Demographic characteristics are shown in Table 44. The diagnoses were made on the basis of history and investigation which included radiology in pancreatitis (endoscopic retrograde pancreatography) and histology in inflammatory bowel disease and gastrointestinal tract malignancy. In all cases intermittent abdominal pain was a prominent feature. None of the patients had a history of hypertension or migraine. None were judged to be depressed at clinical interview by the single investigator and none had

evidence (clinical or biochemical) of chronic hepatic disorder. None were taking antidepressant medication. All were in a clinically stable condition when serotonin was assayed, unchanged over several days. Blood for the assays was drawn fron rested patients between 11.00 am and 15.00pm.

Results and Analysis

Although platelet serotonin has been postulated as a potentially useful biochemical parameter in several disease states the results we obtained did not suggest a consistent change in IBS [Tables 45 - 48], though in such a condition there may be a subset of patients in whom, for example, depression is prominent who might be so identified. It did not help differentiate between IBS and other causes of chronic gastrointestinal symptoms. I did not consider the it appropriate to extend this pilot work particularly given the technical difficulties in specimen collection and analysis.

Table 44. *Subject characteristics for serotonin study*

	n	age	male : female
Irritable bowel syndrome	4	22 - 66	2 : 2
Inflammatory bowel disease	4	19 - 54	2 : 2
Pancreatitis	3	33 - 56	2 : 1
Malignant disease	5	52 - 56	2 : 3

Table 45. *Platelet Serotonin [nmol / l]*

	n	mean	range	SD
Irritable bowel syndrome	4	2067	675 - 3312	1245
Inflammatory bowel disease	4	4203	2468 - 6740	1828
Pancreatitis	3	2789	1515 - 4455	1509
Malignant disease	5	1417	243 - 2833	1208

Table 46. *Platelet Serotonin [nmol / l]*

Differences between the diagnostic groups.

		[1]	[2]	[3]	[4]
				p Student t-Test	
Irritable bowel syndrome	[1]		0.10	0.52	0.54
Inflammatory bowel disease	[2]	*0.11*		0.33	0.03
Pancreatitis	[3]	*0.63*	*0.40*		0.20
Malignant disease	[4]	*0.29*	*0.06*	*0.39*	
		p Mann Whitney U Test			

Table 47. *Platelet Serotonin [pmol / 10^8 platelets]*

	n	mean	range	SD
Irritable bowel syndrome	4	433	153 - 658	262
Inflammatory bowel disease	4	589	418 - 764	156
Pancreatitis	3	835	115 - 1200	623
Malignant disease	5	308	8 - 501	163

Table 48. *Platelet Serotonin [pmol / 10^8 platelets]*

Differences between the diagnostic groups.

		[1]	[2]	[3]	[4]
				p Student t-Test	
Irritable bowel syndrome	[1]		0.34	0.29	0.61
Inflammatory bowel disease	[2]	*0.34*		0.57	0.03
Pancreatitis	[3]	*0.62*	*0.62*		0.28
Malignant disease	[4]	*0.55*	*0.03*	*0.39*	
		p Mann Whitney U Test			

THE INFLUENCE OF ALCOHOL

Symptoms related to alcohol consumption are a common cause of referral to gastrointestinal clinics and such symptoms include abdominal pain and diarrhoea (Langman and Bell 1975). Yet the prevalence of alcohol related problems in IBS patients has been addressed infrequently. Health workers are notoriously inept at identifying or recognising alcohol related problems (Barrison et al 1980). One would expect that in gastrointestinal clinics the recognition of alcohol excess or alcoholism would be improved, and the diagnoses would have to be considered as an explanation for the symptom complex of IBS. Nonetheless it was appropriate to exclude a potential role for alcohol in the symptom complex, particularly given the association between the use of alcohol and psychological disturbance.

The detection of excessive alcohol consumption and alcoholism rests on three main planks ;

1. A careful assessment during routine history taking.

   In some circumstance this can be as effective, or even more effective, than questionnaires, whether these are observer or self-administered. Waterson and Murray-Lyon (1988) found that direct questioning about the usual alcohol consumption level and bingeing was more effective than a CAGE questionnaire in

identifying patients with excess alcohol consumption in the setting of an antenatal clinic.

2. Laboratory parameters.

Several biochemical indices are said to change with chronic alcohol consumption. The most commonly used in routine practice are mean cell volume (MCV) and gamma-glutamyl-transferase (GGT). Others include cholesterol and transferrin. Gamma GT is elevated in 60-80% of 'alcoholics' (Rosalki and Rau 1972), but it can be elevated in many other disease states, and by several medications.

Chick et al (1981) described a correlation between acknowledged alcohol intake and GTT, but a disappointing sensitivity of 54%, and a false positive rate ranging from 10% to 50% in his subject groups (there were three) when used to identify those with alcohol consumption greater than 450g / week (all his subjects were men).

The sensitivity of MCV was even lower : 20% - 40% in a study of 63 well nourished patients with an admitted alcohol intake of more than 80g / day (Wu et al 1974). He reported an MCV of greater than 90fl in 89%. In 29% of patients there was evidence of folate deficiency.

3. Specific interview techniques, largely standardised questionnaires.

The questionnaires which are most commonly used originated in the USA and ask about drinking behaviour and alcohol associated problems, the quantity of alcohol being of lesser importance for these interview techniques. The Michigan Alcoholism Screening Test (MAST) is perhaps the best known (Selzer 1971). But it is somewhat cumbersome, with 24 items, and seen by some patients as threatening. The CAGE questionnaire is a simpler test, consisting of only four questions. [Appendix 7] Derived by Ewing and Rouse (Ewing 1984) during work in a general hospital setting, it has been validated and proved useful in this setting, in psychiatric inpatients (Mayfield et al 1974), in medical outpatients, and in primary care (Wallace and Haines 1985).

CAGE has been criticised for identifying only heavy drinkers and for overdiagnosing those individuals who feel guilty about modest levels of alcohol intake. However Saunders and Kershaw (1980) found CAGE more sensitive than MAST in a community survey.

There is dispute about the relative merits of self-administration vs physician administration of such questionnaires but it seems to have relatively little effect on sensitivity or specificity.

Bernadt et al (1982) found that the GTT did correlate with alcohol consumption, as did the MCV. In 385 patients admitted to a psychiatric hospital he compared the sensitivity of CAGE, MCV and GGT for detecting both alcoholism and excess alcohol consumption.

Sensitivity (% in the category with an abnormal result)

CAGE	GTT	MCV	Diagnostic category
91	33	2	Alcoholism
93	36	0	Excess alcohol

Specificity (% not in the category with a normal result)

CAGE	GTT	MCV	Diagnostic category
77	87	99	Alcoholism
76	87	99	Excess alcohol

The MCV is a tool of very low sensitivity and is therefore of little use in the detection of alcohol related problems. GGT fails to detect two out of three of those with alcoholism or excess alcohol consumption. CAGE detects nine out of ten alcoholics or excess drinkers, but is abnormal in 25 per cent of those who are outwith these diagnostic categories.

Methodology.

The clinical assessment of the 49 patients who comprised the therapeutic trial cohort included routine enquiry about alcohol intake and related problems. In addition the cage questionnaire was administered by the physician (in all cases myself). MCV and GGT were analysed on the baseline blood sample.

Results and Analysis.

No subjects scored more than two on the CAGE questionnaire. Three patients scored two, and seven one. The remaining patients scored zero. The dietician also enquired about alcohol in the 24 hour recall. In none of the recalls was the reported alcohol intake greater than one unit and the dietician commented on possible alcohol abuse in no patients.

There was no correlation between GTT and MCV. [Table 49] Neither GGT, MCV, nor CAGE correlated with the clinical and psychometric assessments shown if Table 51. Nor was an association demonstrated between the parameters of alcohol consumption and general outcome. [Table 50]

It seems that alcohol plays little part on IBS itself. However this is not to deny that gastrointestinal upsets secondary to alcohol intake can mimic the IBS

symptom complex. In the gastrointestinal outpatient clinic awareness of alcohol as a potential problem is high and the fact that none of the patients seemed to have alcohol related symptoms or problems is testimony to the vigorous exclusion of such patients from the IBS diagnostic category in routine clinical evaluation.

Table 49. *Biochemical parameters of alcohol intake.*

	mean	range	SD	r	p
Gamma GT (IU/l)	20.9	2 - 54	9.59		
				-0.13	0.50
MCV (fl)	90.2	85 - 98	3.57		

Table 50. *Biochemical parameters of alcohol intake : relationship with overall outcome. (mean, range)*

	better n = 22		unchanged / worse n = 20	
Gamma GT (IU/l)	21.7	(2 - 49)	20.2	(7 - 36)
MCV (fl)	89.2	(85 - 98)	90.5	(87 - 97)

not significant

Table 51. *Relationship between parameters of alcohol intake and clinical and psychometric assessments. (R)*

		MCV (fl)	GGT (IU/l)	CAGE
anxiety	VAS	0.07	0.17	0.08
	questionnaire	0.10	0.11	0.18
depression	VAS	0.23	0.08	0.21
	questionnaire	0.17	0.13	0.14
initial symptom scores				
	pain	0.04	0.18	0.25
	frequency	-0.12	0.24	0.08
	constipation	0.08	-0.07	-0.28
	global	-0.09	-0.04	0.16
change in symptom scores				
	pain	0.17	0.11	-0.03
	frequency	-0.06	-0.19	0.14
	constipation	-0.15	0.07	-0.21
	global	0.03	0.11	0.09

R = Spearman coefficient of rank correlation not significant

GENERAL PRACTITIONER CONSULTATIONS

As the initial co-actors in the doctor-patient relationship which modulates the future direction and content of the illness behaviour, general practitioners play a pivotal role in determining those patients who are referred to outpatient clinics. This process of selection has a large influence on the characteristics of the patients with a diagnosis of IBS who form the subjects for most studies of the syndrome. Many people who experience IBS 'symptoms' are not referred on by their general practitioner. Presumably within the context of their relationship both GP and patient are satisfied with the agreed explanation and 'reattribution', such that the 'symptoms' are redesignated 'experiences'.

The clinic or hospital doctor misses this all-important, scene-setting interaction and is henceforth disadvantaged in understanding the illness behaviour, having to rely on the face to face account of only one of the actors. Several factors which are considered to modulate consulting behaviour were beyond the scope of this study, but I was interested in whether attendance at an outpatient clinic had a effect on the temporal pattern of attendance or on the principal complaint noted in the GP record. Further I wished to establish whether any change in consulting behaviour was related to psychological scores at the outset or five years later, and to examine the relationship between consulting behaviour, general practitioner records, and self-reported outcome.

In order to assess the patient-general practitioner interaction which produced the hospital referral, the general practitioner medical records of 20 of the IBS patients from the cohort initially examined five years before and described previously, were examined in detail. This was done in the general practitioners surgery by a single investigator with the consent of the GP.

Selection of this small cohort of patients was on the basis of the geographical location of the practice. Only those within two miles of the hospital were included. This restricted the practices to an urban area well served by public transport ; it was thought unlikely that transport considerations would be a notable determinant of reporting / attending / referring behaviour within this area. The patients were drawn from 16 general practices.

The descriptions from the medical records were then compared with those obtained from the postal questionnaire and from the initial assessment five years previously. Each record was examined in full, noting the number of consultations, the formulations of the GP, any prescribed treatment, and any other recorded comments (particularly if they related to emotional or psychological factors, or to specific life events). The index consultation was held to be that of the specialist gastrointestinal clinic.

Consultations were classified according to the principal (first, bold, or underlined) complaint, symptom, or diagnosis.

Gastrointestinal consultations were those in which abdominal pain, bowel habit, dyspepsia, nausea, bloating, fullness, or defaecatory difficulty were predominant. The remaining consultations were classified other. Although this is a somewhat artificial division, particularly given that IBS sufferers often complain of nongastrointestinal symptoms, I wished to examine whether there was a change in this aspect of the presentation with clinic attendance.

Depression and anxiety states were considered to have been diagnosed when they were a part, however minor, of the written record or formulation of the consultation.

The characteristics of the 20 patients were similar to those of the whole group. [Table 52] However of those chosen for detailed examination of their GP notes, only three were in the self reported unchanged or worse category. This renders comparison between the general outcome groups all but impossible. In analysis of the 20 patient cohort the patients are not subdivided into outcome classes.

Table 52. *Subject characteristics. (mean)* *n = 20*

age (years)		38.6
	range	26 - 69
sex ratio (f : m)		14 : 6
high fibre diet at five years		13 [65%]
symptom duration (months)		47.4
	range	3 - 180
initial anxiety score		7.2
	range	0 - 13
five year anxiety score		6.1
	range	0 - 12
initial depression score		5.2
	range	0 - 12
five year depression score		3.4
	range	0 - 10

One image of IBS patients commonly held by hospital-based doctors is of a patient frequently consulting their general practitioner with abdominal or indeed other complaints. However this was nor borne out by examination of the GP record cards.

Table 53. *Temporal relationship between index consultation and number of GP consultations.*

Time from index consultation.	Number of consultations (mean, range)			
	gastrointestinal		nongastrointestinal	
60 - 12 months	5.1	2 - 31	2.0	0 - 18
12 - 3 months	1.0	1 - 10	1.3	0 - 10
3 months - index consultation	3.0	0 - 7	0.7	0 - 7
index consultation - 3 months	0.7	0 - 2	0.3	0 - 2
3 - 12 months	2.5	0 - 8	1.4	0 - 5
12 - 60 months	5.5	0 - 19	1.8	0 - 10

Table 54. *Time to GP reconsultation after index consultation*

	Mean interval before reconsultation	range	number not consulting
gastrointestinal complaint	5.4 months	1 - 18	3
other complaints	6.5 months	4 - 12	5

Five of the patients had had a previous diagnosis of IBS, four in the same GI clinic within the five year preindex consultation study period. The time interval to rereferral ranged from one to four years. Nine of the patients had had a diagnosis of 'dyspepsia' recorded. In three patients there were grounds for suspecting other somatisation reactions - two with 'psychogenic chest pain', one with 'nervous headache'. A specific life event was recorded as being significant for the consultation in five patients at index consultation or within the preceding three months (marital difficulties (2), engagement, housing, worry about employment).

There was no consistent correlation between the frequency of consulting (for gastrointestinal or non-gastrointestinal complaints) and symptoms in the questionnaire.

Likewise there was no clear relationship between GP consulting behaviour before and after the index consultation, and changes in the symptoms between the initial assessment and the five year postal questionnaire.

The complex nature of the relationship between consultations and 'symptoms' was confirmed. Attendance at a gastrointestinal clinic, or some element in the consultation which prompted it, had very little discernable impact on the long term frequency with which IBS sufferers consulted, nor on the predominance of gastrointestinal complaints. There was an early reduction in the frequency of consultation but this was no longer evident after 12 months.

Nonetheless most patients considered the clinic attendance to have been helpful - regretably I did not examine whether the general practitioners shared this view. Taken with the poor correlation between reported symptoms and overall subjective self-assessment, these findings emphasise the difficulty in establishing useful 'outcome measures' in outpatient management of IBS.

Relationship with anxiety and depression

Seven patients had a previous diagnosis of depression or anxiety and two patients had had both diagnostic labels accorded them. These comments were distributed almost evenly throughout the five year period ; median 25 months, range 1 - 52 months.

In the five years after index consultation and clinic diagnosis of irritable bowel syndrome, five patients were thought to have suffered anxiety or depression and one both. Only two of these patients had not previously been within one or other diagnostic category.

Only two patients had received anti-depressant medication in the ten year period. A further four patients had received anxiolytics, exclusively diazepam. One patient had received propranolol for anxiety associated palpitations. Three patients had been referred to a psychiatric outpatient clinic in the five year follow-up period : diagnoses of personality disorder, depression (no antidepressant treatment), and alcohol dependancy were made.

The high incidence of depression and anxiety, often not reported by the

patients themselves, was striking. Its timing seemed unrelated to the index consultation and to the duration of the IBS symptoms.

I found no correlation between the pattern of consultation and either index or five year anxiety scores. [Tables 55,57] The index depression scores showed a weak correlation with gastrointestinal consulting rates though this was notable only for the period before the index consultation. [Table 56] The five year depression rates showed no such correlation. [Table 58] This is further evidence of an association between illness behaviour (GP consulting) and depression scores.

Somewhat paradoxically the psychometric scores at index consultation were a poor guide to previous or subsequent psychiatric diagnosis with no significant difference between the groups of patients. [Tables 59,60] However the trend in each score was for the mean to be higher in those with a previous or subsequent diagnosis of depression / anxiety - perhaps with a greater number of patients this trend would have become a significant difference.

Table 55. *The relationship between GP consultation rates and index anxiety scores. (n = 20)*

	gastrointestinal		nongastrointestinal	
	r	R	r	R
60 - 3 months	0.21	0.31	-0.13	0.38
3 months - index	0.15	0.24	-0.07	0.10
index - 3 months	0.37	0.37	-0.50	-0.45
3 - 60 months	0.20	0.17	-0.11	-0.03
interval (months)	-0.21	-0.12	0.06	0.15

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

not significant

Table 56. *The relationship between GP consultation rates and index depression scores. (n = 20)*

	gastrointestinal		nongastrointestinal	
	r	R	r	R
60 - 3 months	0.75 **	0.54	0.12	0.50
3 months - index	0.68 *	0.53	0.45	0.37
index - 3 months	0.47	0.41	-0.16	-0.29
3 - 60 months	0.20	0.17	0.18	0.21
interval (months)	0.07	-0.04	0.04	-0.01

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

** $p < 0.01$
* $p < 0.05$

Table 57. *The relationship between GP consultation rates and five year anxiety scores. (n = 20)*

	gastrointestinal		nongastrointestinal	
	r	R	r	R
60 - 3 months	0.18	0.44	-0.22	-0.12
3 months - index	-0.14	-0.05	-0.46	-0.5
index - 3 months	0.41	0.47	-0.46	-0.5
3 - 60 months	0.06	0.00	-0.31	-0.42
interval (months)	0.12	-0.08	0.30	0.40

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

not significant

Table 58. *The relationship between GP consultation rates and five year depression scores.*

	gastrointestinal		nongastrointestinal	
	r	R	r	R
60 - 3 months	0.43	0.74 **	0.09	0.07
3 months - index	0.11	0.22	-0.11	-0.16
index - 3 months	0.06	0.06	-0.11	-0.16
3 - 60 months	0.10	-0.14	-0.10	-0.25
interval (months)	0.35	-0.29	-0.01	0.21

r = product-moment correlation coefficient
R = Spearman coefficient of rank correlation

** $p < 0.05$

Table 59. *Index depression and anxiety scores in those with previous depression / anxiety vs those without such a diagnosis.*

	present		absent		
	mean	SD	mean	SD	p
depression	5.4	2.3	4.6	3.5	0.34
anxiety	9.7	2.1	7.1	4.9	0.68

Table 60. *Index depression and anxiety scores in those with subsequent depression / anxiety vs those without such a diagnosis.*

	present		absent		
	mean	SD	mean	SD	p
depression	6.0	3.0	4.8	3.1	0.57
anxiety	9.1	2.7	7.1	5.4	0.56

CONCLUDING DISCUSSION

The difficulties in assessing the response to treatment in IBS are well illustrated by the poor correlation between the subjective general evaluation and the changes in subjective self-recorded symptom scores in the clinical trial. The symptomatic assessment was extensive but objective measures did not include measurement of stool weight nor enteric transit time. Although there is some suggestion that stool weight and transit time correlate with 'diarrhoea' or 'constipation' (Eastwood et al 1984, Cann et al 1983), the balance of evidence is against a clear cut association (Soltoft et al 1981, Oettle and Heaton 1987). There is no correlation between such measures and self-reported symptoms such as abdominal pain and bloating in IBS patients (Hillman et al 1982).

Nor did I study intestinal motility. The use of gastrointestinal motility investigations invests the process of investigation with a degree of invasion and potential morbidity which, though slight, must change the nature of the investigator-subject (doctor-patient) relationship. I wished to avoid this as far as possible in view of my putative contention that this relationship is itself an important element in the behaviour of IBS patients. There is no evidence that motility studies help in the treatment of individual patients, nor that changes with treatment are any guide to the efficacy of the treatment; nor indeed is there evidence even of consistent changes in IBS with treatment. Throughout

I have been concerned with aspects of assessment and management which might prove useful in the routine care of irritable bowel syndrome patients.

Natural History

The study confirms the relatively benign medium term prognosis for IBS patients. The diagnosis is a safe construct with few patients subsequently being accorded an alternative diagnosis or changes in symptom pattern which required review of the diagnosis. Nonetheless there is a substantial minority of IBS patients in whom the symptom complex is a persisting, troublesome feature of their lives.

Fibre intake and fibre supplementation as treatment

Pretreatment dietary fibre intake was, as expected, related to degree of constipation. In the clinical trial the pretreatment levels were certainly not significantly less than in the general population from whom the patients were drawn. The supplement of fibre represented a relatively small addition - perhaps a greater supplement would have had a greater effect. As it was the fibre tablets produced a similar change to that afforded by placebo. However it is a well tolerated treatment as witnessed by the large proportion of patients

continuing with this approach after 5 years. My analysis does not confirm an actual, continuing high fibre diet (or higher than at initial presentation) ; nonetheless that so many patients report this persisting change in lifestyle is surely significant.

Biochemical Indices

The indices I examined offered no prospect of differentiating IBS patients into subclasses which might have afforded insights into shape of the triangle in the proposed IBS model. Nor does it seem likely that they will afford useful diagnostic information.

Psychopathology

Many studies have confirmed the high prevalence of psychopathology in IBS patients. Despite this, formal psychometric assessment is rare in general and gastrointestinal clinics. Reliance on traditional clinical judgement is based in part on familiarity, in part on lack of time, and in part on suspicion (occasionally denigration), of psychological testing. I wished to obtain a reliable, rapid, user-friendly (for patient and doctor) insight into two possibly relevant psychological parameters; depression and anxiety.

The visual analogue scale was easily obtained, and a useful guide to possible psychopathological factors in IBS patients. The results further suggest that the VAS results may be of predictive value, perhaps able to identify those patients who will improve whatever treatment is exhibited.

While in the clinical trial high depression scores seemed to be associated with poor symptomatic improvement (whether this be a true response or a placebo effect), in the five year follow-up cohort anxiety score at five years best differentiated between improved and unimproved groups. One frequently proferred explanation for the latter finding is that in unimproved patients continuing gastrointestinal symptoms fuel persistent anxiety. However, anxiety ratings were not increased over the intervening five years in those who were worse or unchanged, and the outcome groups were indistinguishable with respect to initial and five year gastrointestinal symptoms; their duration, pattern, or severity (with the single exception of abdominal pain). Patients who felt improved reported less pain and less anxiety at five year follow-up than their unimproved counterparts, but these differences did not reflect any other differences in symptomatology.

An alternative explanation is that the sustained anxiety ratings and gastrointestinal symptomatology are both manifestations of a persisting, abnormal perception of stress and gastrointestinal experience in patients who do not improve. Such a hypothesis is supported by the similarity between the

outcome groups in terms of gastrointestinal symptoms and by the observed differences in anxiety ratings.

Other than the duration of follow-up, the striking difference between the three month clinical trial subjects and those in the five year follow-up cohort was the duration of symptoms at initial assessment, reflecting the criteria for recruitment into the short-term therapeutic trial. It is conceivable that anxiety is more involved in the longterm maintenance of the IBS symptom complex, and changes in mood (especially depression) in determining shorter-term fluctuations in perceived distress and illness behaviour in response to life events against this background. Depressed affect would therefore have important implications for response in treatment trials of short duration, but personality traits determining perception of and response to anxiety might modulate the sustained tendency to express the IBS symptom complex as consulting behaviour.

The complex nature of the relationship between consultations and 'symptoms' was confirmed. Taken with the poor correlation between reported symptoms and overall subjective self-assessment these findings raise the question of just what should be useful 'outcome measures' in outpatient management of IBS.

Conceivably the longer-term stability of the consulting behaviour goes hand in hand with with a true reduction in the frequency or severity in experience, or successful reattribution. The consulting behaviour persists as an element in the coping strategy which has now been bolstered by the outpatient clinic consultation. Alternatively the change may lie in the attitude of the general practitioner who no longer feels it nececessary to refer the patient on.

The therapeutic trial confirms the substantial placebo effect which has been previously reported to operate during treatment of IBS patients. The placebo response has been defined as

> *'a psychophysiological effect independent of pharmacological mechanisms'*
>
> (Shapiro 1959-60)

Such a response need not, in general, be limited to subjective experience, though it is this aspect which is most apposite to the present study. Nor is deception a necessary part of the 'placebo response' (Brody 1982) though this too is of lesser consequence in the double blind situation.

The nature of the placebo response has been the subject of much speculation but is is clear that the doctor-patient relationship is a critical component. Adler and Hammet (1973) discuss the importance of the placebo response within the context of various models of illness or distress. They emphasise the transcultural element of the process by which the sick role provides a socially sanctioned respite, and the practitioner (here the physician but elsewhere the healer, priest etc) a coherent, culturally meaningful explanation of the complaints.

These two elements are interactive ; the patients are helped by ;

1. participation in a shared system that seeks to explain the apparently chaotic symptoms.
2. access to a relationship with a culturally sanctioned figure who can offer an explanation for the symptoms and/or behaviour.

The considerable placebo effect highlights the potential central importance of the doctor-patient relationship in the natural history of the IBS symptom complex. In this context it is noteworthy that the placebo effect seems to exert a disproportionately greater influence on the symptom domain of the global score, which seems to have greater import for the general sense of well-being than the experience of pain, or alterations in faecal frequency or consistency.

Perhaps the patients are aware, or become reassured, that the change in bowel habit does not indicate serious underlying disease, but are less well (or less easily) reassured about the benign aetiology of the other symptoms. Bowel habit (its perception and reporting) may be more susceptible to the process of reassurance and reattribution than the other complaints.

The therapeutic impact of the doctor-patient relationship might also underpin the continuing consulting behaviour of IBS patients. It may be particularly important in circumstances in which there is no specific treatment liable to

produce dramatic 'symptomatic' improvement. Thomas (1978) argues that patients may indeed tolerate situations in which no treatment is offered rather better than might be anticipated and that in some such patients find a directive, paternalistic consultation more effective than a sharing consultation style. IBS patients may be particularly disadvantaged by such a sharing approach to consultation : the sharing style may serve to perpetuate the mind - body dualism even though, somewhat paradoxically, it arises out of a concern to promote a holistic, non-paternalistic approach to the patients complaints.

The model of IBS as a behavioural disorder, the characteristics of which are determined by input from three domains which can be considered the points of a triangle (Ford et al 1982), has proved useful. However by delineating the shape and identifying the apices (soma, psyche and circumstance) the model may detract from the essential dynamic nature of the interaction. The points are seen as fixed ; although the shape of the triangle can vary between individuals, and over time in a single individual.

Clearly the psyche apex of the triangle has many inputs and it may be inappropriate to represent it as a single point. Particularly, the findings suggest that the inputs may vary in importance over time. The circumstance apex has proved extremely difficult to examine, and time-consuming examinations of life events are unlikely to gain widespread use in routine clinical practice. The influence of life events on illness behaviour in general and on the IBS symptom complex in particular has proved elusive. Ford et al (1987) suggested that life events operated by causing anxiety in patients who were suffering from a depressive mood disorder.

The soma apex (perhaps best considered in our current understanding as the interaction of dietary constituents and enteric motility) has likewise proved difficult to examine. While the model recognises the input from each apex it

therefore remains difficult to determine the shape of the triangle in any individual patient at any given time. Further the behavioural, dynamic basis of the model is somewhat submerged in the two dimensional representation and the role of past experience and learning are under-represented.

The onset of symptoms in this model of IBS has been explained in terms of Catastrophe Theory (CT). Developed by Thom, CT purports to predict the behaviour of dynamic systems by reference to a limited number of elementary catastrophe models (Stewart and Peregoy 1983). The models configuration is determined by the number of control factors, which are held to represent the topographic axes.

Control factors influence events qualitatively, and independent of their interactions. The 'catastrophe' is a mathematical discontinuity at which point the system moves into another state. It is attractive to picture the discontinuity as the onset of symptoms necessitating medical treatment. However the model is a qualitative one - the axes imply no scale or degree, relative or absolute. It allows little, if any, inference to be drawn on the interactions of the factors, a limitation acknowledged by many proponents of CT. Further, while the change in state can be discontinuous (a catastrophe), an identical position can usually be reached in the model by a non-discontinuous route.

CT has been suggested as a model for a wide range of behaviours. The mathematical basis has been criticised and although it allows elegant

topographical models to be invoked, CT does not help identify the number of aetiological factors, their relative importance, or the way in which they interact in IBS. Further the onset of irritable bowel symptoms is not a discrete event - the process can be seen as a flow through a series of boundaries - experience becomes symptom ; symptom produces consulting behaviour ; consulting behaviour prompts clinic referral.

Nor does the model help predict the natural history or outcome of the symptom complex. Another disadvantages of CT is its perpetuation of the dualistic approach by which psychological states and motor behaviour are separated (they are often represented by diverging axes).

The three domain model may continue to be helpful but it is prudent to consider each domain as the summation of several influences, and the domains themselves as inextricably intertwined. The model can be developed and refined by drawing from the developing discipline of psychobiology the central theme of rhythm or oscillation (Weiner 1989). Traditionally biological systems or functional units have been accorded a homeostatic character, by which the system seeks to preserve its steady state against external or indeed internal stressors. But the steady state belies an oscillating, rhythmic system. Such oscillations are inevitable in systems which depend on feedback loops for control and coordination of homeostatic and other functions. The feedback loops involve a time delay which are one source of the oscillation.

Many systems utilise signals which are themselves rhythmic. Such systems have intrinsic pacemakers by which the frequency, amplitude, and form of the oscillation can be established. A transition from the usual 'steady' state or mode is termed a bifurcation. The base rhythm and the change can be modelled mathematically using nonlinear differential equations (Garfinkel 1983). Dysrhythmic dynamics (chaos) may be almost inevitable in some systems, in others chaotic oscillation may be an unpredictable consequence of external stressors. Chaotic function characterises a subsystem in disease or disorder.

The characteristic feature by which IBS patients are recognised is their behaviour : the function of the system (patient) is paramount, rather than its structure. There are clearly rhythms of gastrointestinal motility, even though their relation to function is not yet well established. Likewise individual mood and emotional states seems to have an inherent rhythm, which have been of particular interest in psychological disorders (Wehr and Goodwin 1981, Vidacek et al 1988). Several of the influences in the IBS symptom complex can therefore be visualised as potentially rhythmic phenomena. The integration of these influences will produce the dynamic we see as behaviour.

It is not be necessary to postulate any major increase in (for example) stress or anxiety - a relatively small absolute change can be amplified by the oscillation(s) or could significantly modulate the overall dynamic. The time scale of the oscillations may likewise be critical - it may determine the frequency within the day or week with which the patient experiences any (or all) of the symptoms. The rhythm may change its ampitude or its frequency - it is interesting to speculate that the former might be true for mood or emotional state, the latter for gastrointestinal motility. Perhaps those people with generally high anxiety levels may respond to changes in circumstance with changes in depression or other inputs such that the system overall (physical and emotional) is dysequilibrated. High baseline levels may be more, or less, resistant to change.

The illness behaviour of IBS can be seen as one aspect of the systems' strategy for establishing a satisfactory function in altered circumstances. Goldberg's reattribution may diminish the amplitude or the frequency of the anxiety or dis-ease engendered by the perceived experience. Perhaps this goes some way to explain the high incidence of placebo response and the reported success with such a wide range of treatment modalities - alterations to diet, hypnosis, behavioural therapy, biofeedback etc. The physician is part of the interaction - his behaviour may be subject to rhythmic changes too and he plays a part in the dynamic function of the system. Consultation with the physician is an integral part of the coping device (Tessler et al 1976). The

medical model, with its emphasis on structure, finds it difficult to accomodate this kind of approach.

The complexity of the forces which forge and maintain the symptom complex and illness behaviour, and the potentially dramatic impact of what seems in isolation a slight change in one potential influence is also explained within this model. The effect of previous experience and learning, and of social and cultural influences are recognised. This model of irritable bowel syndrome can accomodate the heterogeneity of IBS patients and can incorporate most of the elements from the earlier models without losing its own unique identity or validity.

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APPENDICES

Appendix 1

7 Day Diary

Day	1	2	3	4	5	6	7
number of daily bowel movements (0,1,2...)							
type of stool:							
hard broken 1							
pellety 2							
normal 3							
soft 4							
watery 5							
abdominal pain:							
absent 0							
slight 1							
moderate 2							
severe 3							
Remarks							

Appendix 2

DSSI (after Foulds and Bedford)

Recently I have worried about every little thing.
False True
If true this has upset me:
A bit A lot Unbearably

Recently I have been so miserable that I have had difficulty with my sleep.
False True
If true, this has upset me:
Unbearably A lot A bit

Recently I have had breathlessness or a pounding of my heart.
False True
If true, this has upset me:
A bit A lot Unbearably

Recently I have been so worked up that I couldn't sit still.
False True
If true, this has upset me:
Unbearably A lot A bit

Recently I have been depressed without knowing why.
False True
If true, this has upset me:
Fairly Very Extremely

Recently I have gone to bed not caring if I woke up.
False True
If true, this has upset me:
Desperately Very Fairly

Recently, for no good reason, I have had feelings of panic.
False True
If true, this has upset me:
A bit A lot Unbearably

Recently I have been so low in spirits that I have sat for ages doing absolutely nothing.
False True
If true, this has upset me:
Unbearably A lot A bit

Recently I have had a pain or tense feeling in my head or neck.
False True
If true, this has upset me:
A bit A lot Unbearably

Recently the future has seemed hopeless.
False True
If true, how hopeless ?
Completely Very A bit

Recently worrying has kept me awake at night.
False True
If true, this has upset me:
A bit A lot Unbearably

Recently I have lost interest in just about everything.
False True
If true, how much loss ?
Complete A lot A bit

Recently I have been so anxious that I couldn't make up my mind about the simplest thing.
False True
If true, how anxious ?
Fairly Very Extremely

Recently I have been so depressed that I have thought of doing away with myself.
False True
If true, how seriously ?
Complete Very Not very

Appendix 3

Visual Analogue Scales

This is a rather unusual way of trying to find out how you feel. Just to give you the idea I am going to try it out first on finding out how you feel about warm weather. People differ from each other in how they feel about warm weather. Some like it very much. Others can't stand it. Most people of course are somewhere between the two.

Underneath some statements have been placed along a line. I want you to put a mark on the line to show me how you feel about warm weather. You don't have to put it opposite a statement if you don't want to ; you can put your mark anywhere along the line in between statements if you like.

Weather

I dislike warm weather

I like it to be fairly warm

I like the weather to be pretty hot

I like it best when there is a sizzling heat wave

On the next page are two more lines with statements on them, this time about feelings. People often vary in how they feel, so when you are deciding how to mark each line, think about how you personally have been feeling over during the past month.

Remember. Think about how you have been feeling during this past month

Anxiety

I never worry about anything

I get a bit worried occasionally

I often get worried about things

I tend to worry a great deal

I am always in a state of terrible worry and anxiety

Depression

I never feel unhappy

I sometimes feel a bit unhappy

I am quite often in low spirits

I frequently feel very miserable

I always feel very miserable

Appendix 4

Symptom Questionnaire

How many bowel movements do you usually have per day or per week ?

Do you have to rush to the toilet to open your bowels ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Are your motions ever like dry pellets or thin strips ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Are you motions ever watery or unformed ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Do you ever have to strain during a bowel motion ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Do you ever feel the bowel is not quite empty after a bowel motion ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Do you ever experience pain in the tummy ? (that is not your monthly period).

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Is the pain changed by opening your bowels ?

0 never
1 occasionally
2 usually

Is the tummy pain changed by passing wind from the back passage ?

0 never
1 occasionally
2 usually

Does the tummy pain coincide with a change in the shape, consistency or frequency of the bowel motions ?

0 never
1 occasionally
2 usually

Is the tummy pain affected by what you eat ?

0 no
1 yes

If so can you describe how ?

Do you make a conscious effort to eat a diet high in roughage (fibre) ?

0 no
1 yes

Do you ever feel that worry or nerves upset your tummy complaint?

0 never
1 occasionally
2 usually

Do you ever see your GP because of trouble with your nerves ?

0 never
1 occasionally
2 often

Do you use laxatives or purgatives ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

Do you use any medications prescribed by your doctor for your tummy complaint ?

0 never
1 occasionally
2 most months
3 most weeks
4 most days

If so what ?

Have you tried any other method of helping your tummy complaint ?
(eg herbalism, acupuncture, hypnosis ...)

0 no
1 yes

If so what ?

Did it help ?

Since you were seen at the Western General Hospital, have you attended any other clinic with a similar problem ?

0 no
1 one
2 more than one

Do you think your attendance at the Western General Hospital was helpful ?

0 no
1 partially
2 completely

Appendix 5

CCEI

Do you ever feel upset for no obvious reason ?

yes
no

Do you have an unreasonable fear of being in enclosed spaces such as shops, lifts etc ?

often
sometimes
never

Can you think as quickly as you used to ?

yes
no

Have you felt as though you might faint ?

frequently
occasionally
never

Do you find yourself worrying about getting some incurable disease ?

never
sometimes
often

Do you feel that life is too much effort ?

at times
often
never

Do you feel uneasy and restless ?

frequently
sometimes
never

Do you regret much of your past behaviour ?

yes
no

Do you sometimes feel really panicky ?

no
yes

Do you feel uneasy about travelling on buses or the underground even if it is not crowded ?

very
a little
not at all

Do you wake early in the morning ?

yes
no

Would you say you were a worrying person ?

very
fairly
not at all

Do you dislike going out alone ?

yes
no

Do you experience long periods of sadness ?

never
often
sometimes

Do you often feel 'strung up' inside ?

yes
no

Do you worry unduly when relatives are late coming home ?

no
yes

Do you have to make a special effort to face up to a crisis or difficulty ?

very much so
sometimes
no more than anyone else

Have you ever had the feeling that you are 'going to pieces' ?

yes
no

Are you scared of heights ?

very
fairly
not at all

Do you find yourself needing to cry ?

frequently
sometimes
never

Do you have bad dreams which upset you when you wake up ?

never
sometimes
frequently

Do you feel panicky in crowds ?

always
sometimes
never

Have you lost your ability to feel sympathy for other people ?

no
yes

Appendix 6

Platelet serotonin assay

Methodology

Whole blood is taken from the antecubital vein with the patient seated rested. It is added immediately to anticoagulant in a 10ml plain polystyrene tube and spun at room temperature for 10 min at 121 G. The upper two thirds of the platelet rich blood is harvested. Two aliquots are kept ; one for platelet count and one for platelet serotonin.

The remaining plasma is then diluted with Krebs Saline and aliquots of the remainder are preincubated with saline or saline with chlorimipramine to measure passive diffusion. These aliquots are then added do varying concentrations of serotonin in saline, spiked with titritiated serotonin and incubated for one minute at 37°C.

Uptake is stopped by the addition of ice cold chlorimipramine in saline and the tubes spun for 90s at 4000G and 4°C. The supernatants are aspirated, the pellet digested with ammonia solution for 40 minutes, and the aliquot counted.

For platelet serotonin 100 ul of the internal standard for recovery is added to the platelet rich plasma which is incubated for 40 min at 37°C and then frozen at -20°C. The plasma is then thawed, 100 ul perchloric acid /cysteine solution is added and left at 4°C for 15 minutes. The deproteininsed plasma is then spun at 4°C and 100000G for 15 min. The aliquots of the supernatant are taken for direct injection onto the HPLC (25100 ul) and recovery estimation.

Appendix 7

Cage Questionnaire

Have you ever felt you should cut down your drinking ?

Have people annoyed you by criticizing your drinking ?

Have you ever felt bad or guilty about your drinking ?

Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hang-over (eye-opener) ?